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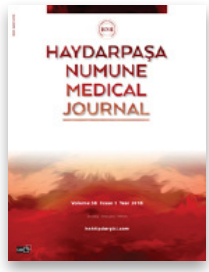

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ORIGINAL ARTICLE

Surgical Outcomes of Intracranial Meningiomas: A Retrospective Study

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Abstract

Introduction: In this study, it was aimed to evaluate the clinical outcomes of patients who underwent surgical resection for meningioma.

Methods: Medical records were retrospectively reviewed for all cranial and spinal cases diagnosed and underwent surgery at BRSHH Hospital between 2012 and 2016. All intracranial meningioma patients constituted the core sample for this study.

Results: This series included 136 (88 females, 48 males) patients, with a mean age of 55.1±14.1 years. The mean preoperative course was 23.0±40.5 months. The most common symptom was headache (71.3%). The most common location was the frontal region which was seen in 29 patients (21.3%). The mean follow-up period was 36.0±18.95 months. 84.4% of grade I, and 68.2% of grade II demonstrated isointense lesions on T1-weighted magnetic resonance imaging (MRIs) (p=0.027). 15.5% of grade I and 47.7% of grade II showed irregularity (p=0.04). Giant tumors were more commonly associated with non-grade I meningiomas than grade I (p=0.006). 58.9% of grade I and 79.5% of grade II meningiomas demonstrated peritumoral edema on MRIs. The presence of preoperative neurological deficit (p<0.0001), irregularity on MRI (p=0.002), and recurrence (p=0.002) were associated with poor prognosis of surgical outcomes. Gross-total resection (GTR) (p=0.0003) was associated with a good prognosis.

Discussion and Conclusion: The presence of preoperative neurological deficit, irregularity on MRI, and recurrence were factors associated with poor prognosis of surgical outcomes. GTR was associated with good surgical outcomes. The presence of preoperative deficits and irregularity on MRIs were associated with a high recurrence rate.

Keywords: Gross-total resection; Intracranial meningioma; Prognosis; Recurrence; Surgical outcome; WHO grade.

Meningiomas are the most common benign intracranial neoplasms[1]. These tumors are extra-axial primary tumors that arise from neoplastic arachnoidal (meningothelial) cap cells in the outer layer of the meninges of the cranial and spinal areas[1-4]. The overall incidence of these tumors in the general population is 2.3/100,000 people[1-4]. Meningiomas rarely occur in children and young adults; these tumors represent 1–3% of all intracranial neoplasms in individuals up to age 20 years and 13.5% of intracranial neoplasms in the 20–34 aged group;[1,4-11] both significantly lower than the incidence in patients over the age of 40[1,4,5,11]. Sex differences between age groups of meningioma are also a well-proven fact; there is a male predominance among patients under the age of 20 years,

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while they are more common in female patients over the age of 20 years[1,5-13].

Meningiomas are categorized by several grading systems but the most accepted grading system was the World Health Organization (WHO) grading system[6,7,14,15]. A higher percentage of meningiomas among radiation-induced patients or those under 20 years are histologically atypical or anaplastic and display aggressiveness, recurrence, and multiplicity[1,4,6,7,8,11,12,16].

Among exogenous factors, radiotherapy is the only exposure that gives an increased risk of meningioma formation[1,2,4,7,12,17]. Previous studies have evaluated the demographics and clinical features of meningiomas[1,5-10]. This study aims to find the prognostic factors that may affect the surgical outcomes and recurrence of intracranial meningiomas by evaluating the midterm surgical outcomes of 136 consecutive cases.

Materials and Methods

Patient Data

Medical records were retrospectively reviewed for all cranial and spinal tumors that were surgically treated in Bakırköy Research and Training Hospital for Neurology Neurosurgery, and Psychiatry (BRSHH) Hospital from January 2012 to July 2016. All intracranial meningioma patients constituted the core sample for this study.

Patient characteristics, such as patient age at the time of surgery, gender, clinical presentation, examination findings, location, WHO grade, histopathological subtype, multiplicity, pre- and postoperative Karnofsky performance scores (KPS), preoperative radiological findings, recurrence rate, surgical outcome, and complication have been evaluated. This retrospective study was approved by the medical Ethics Committee of BRSHH under decision number: 576 on August 2, 2016.

Preoperative Radiologic Assessment

T1-weighted images with contrast, T1-weighted, T2-weighted, and fluid attenuation inversion recovery (FLAIR) images were obtained for all patients. Seven parameters were detected in preoperative Magnetic resonance imaging (MRIs): The largest diameter, the appearance of the tumor on T1- and T2-weighted images, the presence of edema surrounding the tumor, heterogeneity of contrast enhancement, irregularity of tumor shape, and the presence of calcification in the tumor. Peritumoral edema in FLAIR sequences was assessed in 3 groups: (1) Mild edema if the maximum size of the tumor is <2 mm; (2) Moderate edema if the size of edema was between 3 and 5 mm; and (3) Diffuse edema if the size of the edema is >5 mm.

Patient Follow-up

As part of the standard care, the patients undergoing surgical resection for cranial meningioma received routine clinical evaluations and postoperative early CT and/or MRI (in the first 24 h after surgery) as well as MRI during their follow-up visits at 3, 12, 24, and 48 months. In case of the presence of residual tumors after surgery, MRIs were obtained every 3 months. The patient's neurological symptoms and KPS before surgical intervention and at all clinical follow-ups were recorded.

Outcome Measures

Overall survival (OS) time and progression-free survival (PFS) time were calculated using the Kaplan–Meier method for all patients. The date of the last follow-up was used to compute the clinical follow-up period, and the last imaging date was used to determine the radiological follow-up period. Surgical outcomes were divided into two groups; the good prognosis group (which includes all patients who recovered fully from all major symptoms and neurological deficits without new deficits) and the poor/bad prognosis group (which includes improved, unchanged, worsened, and deceased patients).

Statistical Analysis

All data are expressed as the median or mean ± standard deviation with the range shown in parentheses. Univariate analyses are conducted to examine the association between radiological and histopathological features. Differences between groups were assessed by a one-way analysis of variance using the SPSS 25.0 statistical package. Significance in the multivariate model was determined using a $p<0.05$, and trend-level effects were defined as $p=0.05$–0.10. All p values were presented with an odds ratio (OR). When OR could not be calculated, the relative/risk ratio was calculated. The corresponding 95% confidence intervals were obtained. All tests were two-tailed. The study was conducted in accordance with the Helsinki Declaration.

Results

Patients Characteristics

This series included 136 (88 female [64.7%], 48 male [35.3%]) patients between the ages of 2 and 84 years, with a mean age of 55.1±14.1 (median 55, range 2–84 years) years. The

median preoperative was KPS 100 (range, 50–100) for WHO grade I patients, 90 (range, 40–100) for WHO grade II patients, and 55 (range, 50–60) for WHO grade III patients. The most common symptom was headaches (71%), followed by seizures (21%), weakness (14%), and vision disturbances (13%). The most common findings were hemiparesis, hypoesthesia, vision impairment, ataxia, and loss of consciousness, which were seen in 28 (20%), 16 (12%), 15 (11%), 13 (10%), and 11 (8%) patients, respectively. Among 75 patients (55%) who were neurologically intact, 57 (76%) were diagnosed with WHO Grade I and 18 patients were diagnosed with WHO Grade II meningioma. Two patients who were involved in WHO Grade III meningioma were presented with neurological findings (Table 1).

The most common anatomic locations were the frontal, the temporal, and the parietal, which were seen in 29 (21%), 26 (19%), and 23 (17%) patients, respectively. The most common regional location was convexity which was detected in 52 (38.2%) patients. The median size of the largest diameter was 53.5 mm (range: 35–80 mm).

Surgical Resection

Gross-total resection (GTR) was achieved in 107 (79% of all our patients) patients. Among those patients, the extent of resection was Simpson grade 1 in 39 (29%) patients and Simpson grade 2 in 68 (50% of all our patients). Twenty-nine patients (21%) underwent subtotal resection. GTR was achieved in six out of these eight patients. Histopathological examinations revealed that the most common subtype of grade I was transitional meningioma which was

Table 1. Clinical and demographic characteristics of the 136 meningioma patients

	WHO Grade I	WHO Grade II	WHO Grade III
Median age (range) (years)	55 (16–82)	58 (2–84)	66.5 (66–67)
No. of patients (%)	90 (66.2%)	44 (32.3%)	2 (1.5%)
Gender (F/M)	63/27	24/20	1/1
Symptoms - Headache:			
Generalized seizure:	72.2% (65/90)	70.5% (31/44)	50.0% (1/2)
Hemiparesis:	16.7% (15/90)	29.5% (13/44)	0
Vision complaints:	7.8% (7/90)	27.3 (12/44)	0
Vertigo:	15.6% (14/90)	9.1% (4/44)	0
Hypoesthesia:	13.3% (12/90)	9.1% (4/44)	0
Unsteady gait:	10.0% (9/90)	11.4% (5/44)	0
Impaired consciousness:	10.0% (9/90)	6.8% (3/44)	50.0% (1/2)
Aphasia/Dysphasia:	4.4% (4/90)	13.6% (6/44)	100% (2/2)
Fatigue:	1.1% (1/90)	11.4% (5/44)	0
Behavioral impairment:	4.4% (4/90)	2.3% (1/44)	0
Others:	3.3% (3/90)	2.3% (1/44)	50.0% (1/2)
Clinical Findings	–	–	–
None:	63.3% (57/90)	40.9% (18/44)	0
Hemiparesis:	12.2% (11/90)	36.4 (16/44)	50.0% (1/2)
Hypoesthesia:	10.0% (9/90)	15.9% (7/44)	0
Vision impairment:	12.2% (11/90)	9.1% (4/44)	0
Ataxia:	10.0% (9/90)	6.8% (3/44)	50.0% (1/2)
Impaired consciousness:	4.4% (4/90)	13.6% (6/44)	100% (2/2)
Aphasia/Dysphasia:	1.1% (1/90)	11.4% (5/44)	0
Behavioral impairment:	3.3% (3/90)	2.3% (1/44)	50.0% (1/2)
Others:	–	–	–
Preoperative Clinical Course (mos)	3 (0.1–180)	3 (0.5–24)	0.75 (0.5–1)
Preoperative KPS	100 (50–100)	90 (40–100)	55 (50–60)
Postoperative KPS	100 (70–100)	100 (50–100)	75 (60–90)
Clinical Follow-up period* (mos)	42.5 (3–68)	22 (3–68)	56.5 (46–67)
Radiological follow-up period* (mos)	38.5 (1–65)	16 (1–55)	54(42–66)

seen in 55 patients, followed by psammomatous in 10 patients, fibroblastic in 7, and angiomatous in 6 patients. Seven patients were re-operated in our institution for recurrence after surgeries in other centers. The median PFS time among these seven patients was 64 months (range, 8–216 months). The median OS time for these patients was 124 months (range, 84–280 months). The OS rate of these seven patients was 100% during the last clinical follow-up. Two out of them were located in the cerebellum, two in the frontal, two other in the parietal and one in the frontoparietal. Four out of them were resected subtotally, and three were resected totally; one accepted to be Simpson grade I and two were Simpson grade II. Six out of them were diagnosed with WHO grade I (4 transitional and 2 fibroblastic), one patient was diagnosed with atypical meningiomas, but when re-operated in our institution, showed the transformation to WHO grade III after 36 months. One of the rest of the 129 meningiomas showed the transformation from WHO grade II to III next GTR after 12 months.

Seven (3 female and 4 male) patients were diagnosed with meningiomatosis (the patients who showed multiplicity, i.e., more than one meningioma on presentation). Three of them had 3 lesions, while four had 2 lesions. Only the biggest lesions were treated surgically, two of these surgically treated lesions were recurrent and treated surgically, followed by Gamma Knife. The median age of these seven patients was 67 (range, 35–80). The median size of the largest diameter was 51 mm (range, 29–66 mm). Six patients were diagnosed with atypical meningioma and one with transitional WHO grade I. Thus, there is association between meningiomatosis and non-grade I meningioma (p=0.006; OR=13.4 "1.6–114.6").

Preoperative MRI Findings

The median largest diameter was 42 mm (range, 17–80 mm) for grade I, 45 mm (range, 23–80 mm) for grade II, and 77.5 mm (range, 55–100 mm) for grade III meningiomas. According to the largest diameter of the lesion, we divided the patients with meningioma into three groups; medium (17–38 mm), large (39–60 mm), and giant (>60 mm). Giant tumors were more commonly seen in non-grade I meningiomas than grade I meningiomas. 7% (n=6) of grade I meningiomas were giant, while 23% (n=10) of grade II and one (50%) of two anaplastic meningiomas were giant (p=0.006; OR=4.4 "1.5–12.8"). Seventy-one percent of grade I meningiomas (64/90) demonstrated hyperintensity on T2-weighted sequences and 65.9% of grade II meningiomas (29/44) demonstrated hyperintensity on the same sequences (p=0.56; OR=0.76 "0.36–1.63"). Fifty-nine percent of grade I meningiomas (53/90) demonstrated diffuse or moderate peritumoral edema (the thickest diameter >2 mm) on FLAIR MRI, while 79.5% of grade II meningiomas (35/44) demonstrated diffuse or moderate peritumoral edema (p=0.035; OR=2.5 "1.1–5.7"). This means that non-grade I meningiomas are more likely to demonstrate diffuse or moderate peritumoral edema on FLAIR sequences rather than grade I meningioma. Eighty-four percent of grade I meningiomas (14/90) showed heterogeneous enhancement on T1-weighted images and 77.3% of grade II meningiomas (10/44) showed heterogeneous enhancement on the same sequences (p=0.25; OR=1.7 "0.7–4.1").

Surgical Complications

17 (12.5%) patients developed various complications after surgery. The most common complication was a new generalized seizure, which was observed in seven patients (5%). Six patients (4%) experienced early postoperative hematoma; four of them were re-operated to remove it. Five patients developed new neurological deficits. Two patients were readmitted for increased postoperative edema and were treated conservatively with steroids. Two patients experienced hydrocephalus and both of them underwent surgery to place a ventriculoperitoneal shunt. Surgical site infection was observed in two patients. Both of them were treated with antibiotics. One patient had a postoperative infarction. Two patients died; one experienced postoperative hematoma and re-operated, but died 50 days later after having meningitis, and the other's neurological condition deteriorated and subsequently died 8 months after her postoperation.

PFS and OS Times

The mean follow-up period was 36.0±18.9 months (range from 3 to 68 months) (Table 1). After excluding seven patients who were previously operated on in other institutions and re-operated on in our institution after recurrence, the mean PFS period was 33.1±21.3 months (range from 50 days to 68 months). The median PFS period was 30.5 months. Progression-free rate was 92.3% (n=119/129). The mean OS period was 35.5±19.8 months (range from 50 days to 68 months). The median OS time was 35.5 months. 98.4% (n=127/129) of the patients were still alive at the end of the last follow-up time.

Factors Affecting Surgical Outcomes

The median postoperative KPS was 100 (range, 70–100) for WHO grade I patients, 100 (range, 50–100) for WHO grade II patients, and 75 (range, 60–90) for WHO grade III patients.

Table 2. The characteristics of recurrent meningioma patients

Sex	Age (yrs)	Symptoms; Preoperative neurological deficits	Tumor location	The largest diameter (mm)	PreO edema and irregularity on MRI	Resection extension and Simpson grade	Follow-up and PFS (mos)	Tretment of recurrence	Outcome	WHO grade and subtype
M	56	Headache, hypoesthesia, and unsteady gait; Deficit (+).	CPA	44	Minimal; Irregular	GTR; Simpson grade II	57; 48	Re-operated; GTR- Simpson II	Good	I; Psammomatous
M	73	Headache, hemiparesis, and nausea; Deficit (+).	Frontal	52	Diffuse; Irregular	STR; Simpson grade III	50; 24	Gamma knife	Good	II; Atypical
F	71	Behavior changes; Deficit (+)	Olfactor groove	80	Diffuse; Irregular	GTR; Simpson grade II	49; 36	Gamma Knife	Worsened	I; Psammomatous
M	66	Loss of consciousness and hemiparesis; Deficit (+)	Frontal	100	Moderate; Irregular	GTR; Simpson grade I	45; 24	Gamma Knife; re-operated; re-gamma knife	Improved	III; Anaplastic
F	73	Headache and reduced vision in lt eye; Deficit (+).	Temporal	42	Moderate; Regular	STR; Simpson grade III	30; 24	Observation; Bad general status	Unchanged	II; Atypical
F	62	Loss vision in Rt eye; Deficit (+).	Temporal; sphenoid wing	45	Diffuse; Irregular	STR; Simpson grade III	20; 9	Gamma knife	Unchanged	I; Psammomatous
F	66	Hemiparesis; Deficit (+).	Frontoparietal	34	Diffuse; Irregular	GTR; Simpson grade II	18; 14	Gamma knife	Unchanged	II; Atypical
M	61	Headache, and hemiparesis; Deficit (+).	Parietooccipital	61	Moderate; Irregular	GTR; Simpson grade II	10; 3	Re-operated followed by RTP	Good	II; Atypical

M: Male; Female: Female; PO: Postoperative; PreO: Preoperative; mos: months; yrs: years; GTR: gross-total resection; CPA: cerebellopontine angle; PFS: progression-free survival time; RTP: radiotherapy.

110 patients recovered (good results), 2 patients improved, 17 patients unchanged, 5 patients worsened, and 2 patients died. Presence of preoperative neurological deficit (p<0.0001; OR=28.8 "6.5–127.5"), irregularity on MRI (p=0.002; OR=4.2 "1.7–10.4"), and recurrence (p=004; OR=10 "2.2–45.8") were associated with poor prognosis. GTR (p=0.0003; OR=5.9 "2.3–14.9") was associated with a good prognosis. According to our results, we found that age and gender, tumor site, the largest diameter of the tumor (p=0.74), WHO grade, the presence of preoperative peritumoral edema, and Simpson grade I (aggressiveness of surgery) had no impact on surgical outcomes.

Clinical Outcome and Follow-up

There was no relationship between the presence of seizure and both of peritumoral edema (p=0.27; OR=0.57 "0.22–1.45") and WHO grade (p=0.12; OR=1.97 "0.84–4.6"), but the supratentorial location of tumor was associated with the presence of seizure (p=0.048; OR=0.17 "0.02–1.36").

After excluding the seven patients who were operated on in other institutions initially and the patient who died (n=2), recurrence was seen in 6.3% (n=8) of the patients. The median PFS time was 24 months (range, 3–48 months). The characteristics of patients with recurrent meningioma are given in Table 2. The presence of preoperative deficits and irregularity on MRIs were associated with a high recurrence rate.

Discussion

Meningiomas are extra-axial, well-circumscribed, and usually slow-growing neoplasms. These tumors can occur in patients of any age but are commonly present in middle age. Females are more likely to develop an intracranial meningioma, with a female/male ratio of approximately 2:1[12,13-20]. Older patients tend to have sporadic meningiomas, while patients under the age of 20 years tend to have meningiomas associated with genetic syndromes[1,2,5,7,9,11]. We have two female patients in our series diagnosed in their childhood. None of our patients had genetic syndrome or the etiology of radiation.

Several studies suggested that convexity is the most frequent location for adult intracranial meningiomas[1,21,22]. On the contrary, some authors report that intraventricular and infratentorial meningiomas are more common in children[5,6,8,9]. In our series, 38.2% (n=52) of our cases were located in convexity.

High-grade meningiomas are characterized by high tumor cellularity, increased nucleus/cytoplasmic ratio, increased mitotic cells, and small tumor cell size, and these characteristics can lead to larger tumors, shape irregularity, and as a result, increased peritumoral edema[23]. In the current study, irregularity of tumor shape, peritumoral edema (>2 mm), giant tumor at presentation (>60 mm), and multiplicity were all significant predictors of WHO non-grade I meningioma. The isointensity of the lesions on T1-weighted MRI sequences was a significant predictor of WHO grade I meningioma. A recently published study[23] suggested that peritumoral on T2-weighted, heterogeneity on T1-weighted enhanced MRI, and irregular shape of tumor were all significant predictors of WHO non-grade I meningioma.

In our results, the presence of heterogeneity and calcifications did not accurately predict the aggressiveness of meningioma. In contrast, the presence of irregularity, abundant peritumoral edema, and multiplicity demonstrate the aggressiveness of meningioma. Insight of this, the approach of tumor has to be planned according to meningioma's appearance on MRI.

In our series, we select the observation option for meningiomas whose largest diameter is <15 mm and those that are asymptomatic and not growing. For medium, large, and giant meningiomas that cause significant mass effects on adjacent parenchymal tissue, we prefer Simpson-grade I surgical resection[18,19,21-23]. In cases where the dura cannot be removed, it is coagulated, constituting a Simpson grade II resection[18,19,21-23]. Large and giant lesions that invade or are intimately associated with critical structures such as the cavernous sinus or nearby lower cranial nerves may be debulked, and the residual component followed up with radiographic imaging studies or treated with gamma knife or radiotherapy in the event of radiographic progression[24]. In this study, we used gamma knife or radiotherapy as adjunctive treatment after subtotal resection if there was a high recurrence risk. In this series, radiotherapy was applied in eight, and gamma knife was applied in fourteen cases.

Superficial convexity lesions have significantly lower surgical-related morbidity than skull base lesions that are in proximity to critical neurovascular structures[1]. In our study, 17 patients (12.5%) experienced various complications. We investigated the factors that may facilitate new seizure occurrence and we found that variables such as age and gender of the patient, tumor site, WHO grade, presence of preoperative peritumoral edema, and extent of resection had no association with new postoperative seizures.

Recurrence after surgery is related to the extent of resection and the WHO grade of the tumor[1,25]. One recent study[1] supposed that the recurrence was more common with skull base tumors as the authors were not able to achieve a complete resection for patients with skull base supratentorial convexity meningiomas. In contrast to what is reported in the literature, our results demonstrated that preoperative deficits and irregularity on MRIs were associated with a high recurrence rate, while age and gender of the patient, tumor size and site, WHO grade, presence of preoperative peritumoral edema, the extent of the surgical resection and Simpson grade had not influenced the progression of the tumor (recurrence).

The study has several limitations: first, it is a retrospective study that may suffer from inherent bias. Second, the sample size of our cohort is small, and third, the follow-up period is not long enough to make generalizations for PFS and OS periods. Further prospective studies with a larger sample size are needed to validate our results.

Conclusions

GTR for the treatment of meningioma grade I and II is enough without necessary adjuvant treatments; GTR with preservation of neurological functions is the best treatment to relieve patients' complaints and reduce the recurrence rate. Grade I meningiomas are more likely to demonstrate isointense on T1 sequences rather than grade II-III meningiomas. Non-grade I meningioma is more likely to demonstrate diffuse or moderate peritumoral edema on FLAIR sequences rather than grade I meningioma. The presence of preoperative neurological deficit, irregularity on MRI, and recurrence were factors associated with poor prognosis of surgical outcomes. GTR was associated with good surgical outcomes. The presence of preoperative deficits and irregularity on MRIs were associated with a high recurrence rate.

Ethics Committee Approval: This retrospective study was approved by the medical Ethics Committee of BRSHH under decision number: 576 on August 2, 2016.

Peer-review: Externally peer-reviewed.

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