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Research Article

Efficacy of Gamma-Knife Radiosurgery in Grade 2 and Grade 3 Meningioma: A Single-Center, Long-Term Follow-Up Study

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Abstract

Objectives: Gamma-Knife Radiosurgery (GKR) is a safe and effective treatment option in patients who have a high risk of complications in skull base and eloquent area-based tumors, in those to whom total surgery cannot be applied. The purpose was to analyze the results of radiosurgery in patients who underwent GKR for the residues or recurrent tumors in high grade meningiomas.

Methods: A retrospective screening was performed on patients who underwent GKR at Gazi University between 2004 and 2018. The gender, mean age, location, volume, complications, size changes after GKR were noted.

Results: A total of 35 (79.5%) patients were treated with Grade 2, and 9 (20.5%) were treated with Grade 3 meningiomas. The mean follow-up period was 48 months (3-108). The mean volume was noted as 9339 mm^3. The tumor control rates after GKR were determined as 94% in Grade 2 and 55% in Grade 3 meningiomas.

Conclusion: GKR can be applied as a safe and effective method for postoperative tumor control in high grade meningiomas.

Keywords: Atypical meningioma, high-grade meningioma, malignant meningioma, radiosurgery, gamma-knife

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The term Meningioma was first used in 1922 by Cushing.[1] Meningiomas are among the most commonly diagnosed primary brain tumors.[2] They originate from the meningothelial cells of the arachnoid. According to the World Health Organization classification, meningiomas are divided into 3 classes as Grade 1, which constitute approximately 80% of all meningiomas, and which has a slow growth pattern and a low recurrence rate of (10% in 5 years); Grade 2, which has a recurrence rate of 30-40% and which constitute 20% of all meningiomas; and Grade 3, which has a recurrence rate of 20% and which constitute 50-80% of all meningiomas.[3, 4] In the emphasis made by the European Association of Neuro-Oncology guidelines, Simpson grade 1 Resection is the first option in meningioma treatment.[4, 5] Gamma Knife Radiosurgery can be applied effectively and safely as an alternative and complementary treatment method when surgery cannot be performed because of the featured brain structures around the localization. It was shown in many studies that Stereotactic Radiosurgery is effective in terms of tumor size control and low complication rates.[6, 7]

The purpose of the present study was to examine the ef-

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fects of the radiosurgery applied in meningioma cases on progression control or on ensuring regression in patients diagnosed with WHO Grade 2 or Grade 3 Meningioma.

Methods

In the present study, we retrospectively scan the data of 817 patients who underwent GKR treatment with meningioma diagnosis at Gazi University Gamma Knife Center between 2004 and 2018. In the study, the mean age, gender, location, symptoms, volume, the rate to which the treatment can be applied, follow-up durations, and complications were documented.

Radiosurgery Technique

Gamma Knife Radiosurgery was applied by using Leksell Gamma Knife Model C and Perfexion (Elekta Instrument EU, Stockholm, Sweden). The 1-mm contrast T1-weighted images were adapted to the system in the planning unit over 3-Dimension in axial coronal and sagittal. The tumor volumes were calculated by using the Osiris Program (version 4.8; Service of Medical Informatics, Geneva University Hospital, Geneva, Switzerland). The average dose was administered as 14.2 Gy (range 4.5-22).

Patient Follow-Up Period

The follow-up of the patients was carried out at Gazi University Gamma Knife Unit in a 3-month period. The follow-up of the stable patients was carried out with a 6-month cycle. The neurological examinations and radiological evaluations of all patients who came to the follow-up were compared with pre-intervention examinations and images. According to the treatment size, those below 90% were considered to have shrinkage, those above 110% were considered to have growth, and those between 90-110% were considered as stable.

Statistical Analysis

The descriptive statistics were carried out in all series and in all subgroups for all the parameters (Table 1). In the multivariate statistical studies, the impacts of age, gender, localization, treatment doses, and tumor volume on post-treatment progression and on complications were examined in all series and subgroups. The Kaplan-Meier Analysis was made for survival without progression in 36, 48, 60 and 96th months.

Results

In the 817 patients who were scanned, 44 (5.3%) patients were identified as Grade 2 and 3, and those with Grade 1 pathology levels were excluded from the study. The treatment was applied to 35 (79.5%) patients with Grade 2 meningioma diagnosis; and 24 (68.5%) female and 11 (31.5%) male patients were noted. The mean age was 47.9 (range 18-80), and the mean follow-up time was 49.9 (range 3-100)

Table 1. Demographic characteristics of patients

Distribution of Grade 2 and Grade 3 Meningioma Patients Undergoing Gamma Knife Radiosurgery			
	Grade 2	**Grade 3**	**p**
Female/Male, n (%)	24 (68.5)/11 (31.5)	4 (44.5)/5 (55.5)	0.116
Mean Age	47.9	55.1	0.531
Mean Follow-Up Period	49.9	46.5	0.368
Treatment Before Gamma Knife, n (%)			
Surgery	35 (100)	9 (100)	0.014
Radiotherapy/Gamma Knife	5 (14.2)	5 (55.5)	
Mean Tumor Volume	6931 mm^3	18708 mm^3	<0.01
Mean Dose	14.2 Gy (12-16 Gy)	16.5 Gy (14-20 Gy)	<0.01
Complication, n (%)			
Loss of Vision (Temporary)	7 (0.9)		
Narrowed Vision	1 (0)		
Loss Of Hearing	2 (0)		
Fascial Paralysis (Temporary)	2 (0)		
Motor Deficit	1 (0)		
Cranial Nerve Paralysis	8 (1)	1 (11.1)	
Tumor Size Control, n (%)			
Unchanged	28 (80.1)	5 (55.5)	0.223
Decrease	5 (14.2)		
Increase	2 (5.7)	2 (22.2)	

months. A total of 23 (65.7%) patients were operated on once; 8 (22.8%) patients were operated on twice, and 4 patients (11.4%) 3 or more times. A total of 5 (14.2%) patients underwent conventional radiotherapy before GKR. Two (5.7%) patients were administered Gamma Knife once. The mean tumor volume was 11282 mm^3, the mean dose was 14.3 Gy, and the rate of the radiated tumor was calculated as 94.8% (range 60-100%). Five (14.2%) of the patients had reductions in tumor size, 2 (5.7%) patients had an increase in size, and 28 (80%) patients had no differences in tumor size. Non-specific symptoms (headache, tinnitus, vertigo) were observed in 5 (14.2%) patients after Gamma Knife. A total of 30(85.8%) patients did not have any complications.

Nine (20.5%) patients were treated due to Grade 3 meningioma diagnosis. Four (44.5%) female and 5 (55.5%) male patients were noted. The mean age was 55.1 (range 40-71), the mean follow-up time was 46.5 (range 15-86) months. All patients were operated 2 or more times. Five (55.5%) patients underwent Conventional Radiotherapy before GKR. The mean tumor volume was 18708 mm3, the mean dose was 16.5 Gy, and the rate of the radiated tumor was calculated as 96.1% (range 74-100%). Two (22.2%) patients had progression in their tumor sizes. Two (22.2%) patients underwent surgery after GKR. Five (55.5%) patients had no differences in their tumour sizes. One (11.1%) patient had hemiparesis after GKR.

The flow chart is given in figure 1 and the distribution of all patients is given in Table 1, and their localizations are schematized in Table 2.

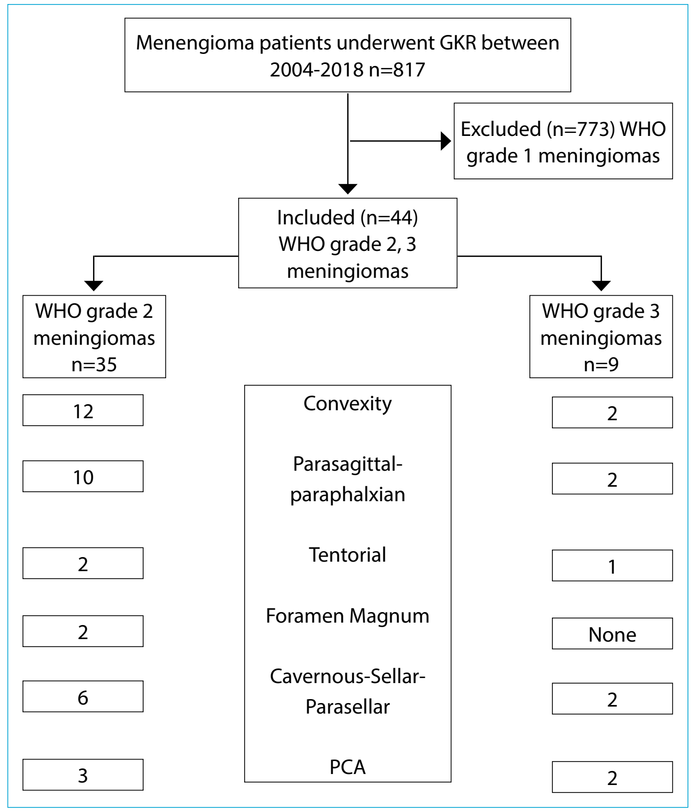

Figure 1. The flow chart figure.

Discussion

The present study, which was conducted in single cente, is among the studies conducted with the highest number of patients in terms of Atypical Meningiomas. With the addition of radiosurgery to gross total resection, the rate of recurrence decreases, and tumor control is achieved. In meningiomas, surgical treatment still has priority. Stereotactic Radiosurgery option may be applied because of adhesions to the localization, size and surrounding tissue, because it results in limited resection, or if patient refuses to undergo surgical treatment. GKR is a treatment method that is often completed in one single session. Haselberger et al. reported in a 2009 study that patients undergoing Stereotactic Radio Surgery had fewer hospital processes than in Beam Radiotherapy or Microsurgery.[8] Patients are treated daily in our clinic, and the mean hospitalization period is 6 hours. The internal hospital processes of the patients are kept to a minimum by performing the follow-ups in clinical conditions.

Table 2. Distribution of the tumor localization areas

Distribution of Tumor Localization Area of Grade 2 and Grade 3 Patients Undergoing Gamma Knife Radiosurgery			
	Grade 2, n (%)	**Grade 3, n (%)**	**Total**
Convexity	12 (85.7)	2 (14.3)	14
Paraphalxian-Parasagittal	10 (83.3)	2 (16.7)	12
Petroclival	0	0	0
Tentorial	2 (66.7)	1 (33.3)	3
Foramen Magnum	2 (100)	0 (0)	2
Cavernous – Sellar - Parasellar	6 (75)	2 (25)	8
Sphenoid wing	0	0	0
Ponto-cerebellar angle (PCA)	3 (60)	2 (40)	5

In previous studies, the margin dose ratio varied in the range of 12-16 Gy. In applications under 12 Gy, it was noted that the tumor control rate was suboptimal, and that symptoms that could develop after the application might increase in higher doses.[8-15] In our study, the margin dose was 14 Gy, which is in line with the previous studies in the literature.

In Meningiomas, the basic purpose of the Stereotactic Radiosurgery is to control tumor growth and to maintain neurological functions.[16] There is a consensus that it is more effective in sizes 3 cm and below.[17,18] In our study, the tumor control rate was found to be 98%. In many previous studies, the tumor control rate was found as above 90%. Kondziolka et al. conducted studies between 1999 and 2008, and found as a result of a 10-year follow-up that the tumor control rate was 91% for Grade 1, 50% for Grade 2, and 17% for Grade 3.[19, 20] In our study, the control rates were 96% in Grade 1, 94% in Grade 2, and 55% in Grade 3 during the follow-up process.

In Atypical and Malignant Meningiomas, the manifestation is a little more dramatic. In patients who do not undergo additional treatments after the surgery, recurrence rates are as high as 38% for Grade 2 and 78% for Grade 3[21] before 5 years. Aizer et al. published an article in 2015 and reported that the 5-year survival rate after Stereotactic Radiosurgery applied to Atypical Meningioma was 78.2%.[13] In the study of Wang et al., the 5-year survival rate was found to be 88.9% for Grade 2, and 66.7% for Grade 3. In the same study, the recurrence rate was 20.4% for Grade 2, and 25.4% for Grade 3.[15] In the 52-patient series of Mattazo et al., a 3-year tumor control rate was 100% for Grade 2 and 0% for Grade 3.[22] Pollock et al. published an article in 2012 and reported the post-radiosurgery 5-year tumor control rate as 40% in malignant-formation meningiomas.[23] The 94% control rate for Grade 2, and 55% control rate for Grade 3, which were determined in the present study, are considered to be significant results for survival and recurrence. Kano et al. suggested in 12-patient series that high-dose radiosurgery (20 Gy) would be better in controlling high-grade meningiomas.[24] In our study, a higher dosage of treatment was performed than in benign meningiomas. The margin dose for Grade 2 was 16 Gy, and 20 Gy for Grade 3.

Hardesty et al. showed a 25% recurrence in atypical meningioma in their series. Ferraro et al. reported the 3-year tumor control rate as 70.1% in radiosurgery applied to Grade 2 Meningioma patients who were operated.[25] Again, in a study conducted on Grade 2 patients, a similar rate of 68.9% was found.[26] They showed that the tumor control rate was 100% in 73-month follow-up after radiosurgery after Gross Total Resection.[14] These rates support our study.

Our only patient whose neurological examination regressed was grade 3 meningioma and the location was close to the motor cortex (convexity meningioma). He had been operated twice before radiosurgery and despite receiving radiotherapy, tumor volume progression was detected. This patient was the patient with the largest tumor volume in our study. In the literature, it is seen that as the tumor volume increases, the tumor control of radiosurgery decreases, the complication rate increases and is similar to our study.[5,6]

Considering 6 patients (2 grade 2, 4 grade 3) with increased size after radiosurgery, one of these patients was convexity, 3 of these patients were parafalcine-parasagittal, and 2 of them were cavernous-sellar-parasellar (Fig. 2). When we look at Simpson's surgical staging, it was stage 4 and 5, that is, recurrence rates were 45% and 60% in 5 years, respectively.[5,6] It was not surprising that the size increases were observed in parafalxian-parasagittal and cavernous-sellar-parasellar tumors that could not be surgically operated in Simpson stage 1 and 2 due to their location, had relatively higher tumor volumes, and also could not be performed with high-dose radiosurgery due to their proximity to anatomically important and sensitive structures.

Limitations

As a result of retrospective studies, our study has some limitations. In parallel with our radiosurgery experience over time, the change in our treatment dose and planning strategies is a limitation in this study, especially with a long follow-up period. Another is that we use Gamma Knife Model C until 2013, and we use Gamma Knife Perfexion since 2013, even though it does not cause any statistical changes.

Conclusion

Gamma Knife Radiosurgery is a treatment method that can be applied safely in meningioma patients. In groups of patients in whom the surgical complication rates are high, who require additional treatment due to residual surgeries, and/or in patient who refuse surgical treatment, it is an effective and safe treatment method with tumor control rates as 94% and 55%, respectively in Grade 2 and Grade 3 meningiomas, reducing the hospital process of patients after applying daily compared to other methods, in extending the recurrent time of high-grade tumors or in providing tumor control.

Disclosures

Ethics Committee Approval: This study was conducted in compliance with the ethical principles according to the Declaration of Helsinki, and it was approved by the local Institutional Review Board (Number: 2021/83).

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Conflict of Interest: None declared.

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