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Outcomes of Gamma Knife Radiosurgery in Patients with Parasagittal Meningioma

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Abstract

Background & Aim: Treatment of parasagittal meningioma (PSM) is always a challenge, especially if the tumor is spread enough to invade critical structures like venous sinuses. This study aims to evaluate the outcomes of gamma knife radiosurgery in patients with parasagittal meningioma.

Materials & Methods: In this descriptive retrospective study, medical records of 61 patients with PSM who had undergone GKRS from 2003 to 2013 were reviewed. The demographic characteristics, medical history and radiotherapy history, tumor's volume and the characteristics of radiosurgery were assessed. Radiological tumor control following treatment were evaluated during follow-up period.

Results: In this study, 32 patients (52.5%) were men and 29 (47.5%) were women. Of 61 patients, 45 had a history of surgery or/and radiotherapy. The mean tumor volume was 11.35±9.20 ml (1-37.9 ml). The mean follow-up time was 30.28±27.48 months. Five patients died. Radiologic tumor control was achieved in 91.8% of the patients, in whom the tumor volume decreased to 30 (49.2%) and remained unchanged in 26 (42.6%) ones. The tumor volume increased in 5 patients (8.2%). Overall, the progression-free survival of the patients was 98.6% during 12 and 67.04±13.4% during 60 months. Edema occurrence rate was 18%. There was no significant difference in GKRS characteristics, tumor volume, and history of surgery and radiotherapy between patients whose tumors were controlled and patients who experienced an increase in the tumor volume.

Conclusions: Our study suggest that GKRS can be the first or second treatment to control PSM. There was no association between the treatment outcome, tumor characteristics, and radiosurgery parameters AS radiosurgery management in PSMs encounter limitations , a long-term follow-up to diagnose life-threatening complications including brain edema is needed.

Keywords: Radiosurgery, Parasagittal Meningioma, Superior Sagittal Sinus, Treatment Outcome, Cerebral Edema

1. Introduction

Parasagittal meningioma (PSM) is the second most common region of intracranial meningiomas accounting for 21-31% of all (1). Management of PSM may be complicated because of its partial or complete invasion to adjacent critical structures, particularly, the superior sagittal sinus which can cause severe brain edema and venous infarction (1). Although surgical resection of tumor is the first line of treatment for meningiomas, gamma knife radiosurgery (GKRS) has been proved as an appropriate alternative in the last decades. There is a higher risk of morbidity and mortality following open surgery of PSM. Therefore, using gamma knife can prevent the various risks of surgery such as bleeding, infection and permanent neurovascular complications (2, 3).

However, GKRS is still accompanied by such morbidities due to its radiation effects on susceptible adjacent structures, most notably the superior sagittal sinus wall and lumen as well as the veins affected in radiation field (2). It has been revealed by literature that PSMs are at a particular risk for venous occlusive complication, which leads to brain edema, especially in comparison with skull-base lesions (2, 4, 5).

Considering the value of stereotactic radiosurgery in PSMs, which has been under debate recently, we performed this study to evaluate the outcomes of GKRS in patients with PSM in Iran Gamma Knife Center.

2. Material and Methods

2.1. Study design

In this descriptive, retrospective cross-sectional study, we reviewed the records of 61 patients with parasagittal meningioma diagnosed and confirmed by either CT scan or MRI who underwent GKRS from 2003 to 2013. The study was conducted in Iran Gamma Knife Center, Tehran.

2.2. Data Collection

The hospital records of patients who had survived were examined to collect the demographic characteristics and medical history data including age, sex, primary clinical signs and symptoms, underlying diseases, radiosurgical parameters such as the maximum dose, marginal dose, isodose, and mean follow-up time. Tumor size and volume were recorded according to MRI reported by two expert radiologists. The exclusion criteria were not attending follow-up visits, multiple meningioma, a history of other brain tumors, age below 18 years old, and use of fractionated GKRS.

After GKRS, the patients were assessed by MRI every six months in the first year and then every year, for three years routinely

The gamma knife device was the Elekta Model C, Version 5.34, and Type C. To perform GKRS, after preparing the patient, the stereotactic frame was attached to head using four pins with a depth of about 2 mm. Then MRI, CT scan, or brain angiography was done to achieve appropriate stereotactic images. All tumor characteristics including its volume and distance from sensitive points were determined accurately and used in designing the treatment plan. After designing, the gamma knife device, which was a hemisphere comprising 201 cobalt sources and 60 radiation directions, was used.

In this study, we assessed the radiological outcome of treatment including tumor volume in last follow-up after treatment. Moreover, we evaluated the determinants and short-term complications including headache, vertigo, nausea and muscle weakness following GKRS as well as the patients' progression-free survival(PFS).

2.3. Statistical analysis

Descriptive statistics was used to analyze demographic and clinical data. Quantitative variables were reported as mean ± SD and qualitative variables presented as percentage and ratio. A Kaplan-Meier plot was constructed to assess progression-free-survival. All statistical analyses were performed using SPSS (version 22.0) and p-value less than 0.05 was considered as statistical significance.

3. Results

Sixty-one patients with parasagittal meningioma were evaluated, of whom 32 were men (52%, mean age: 49.70±16.95 years old) and 29 were women (47.5%, mean age: 52.19±13.05 years old). There was no significant difference in age and sex between participants. Moreover, 45 patients (73.8%) had a history of surgery and 16 (26.2%) had no previous surgery or radiotherapy in their history. Of 45 patients with a history of surgery, 30 patients had one, nine had two, and five had three times of operation. Four patients with a history of surgery also received postoperative radiotherapy. Primary symptoms were headache (37%), seizure (22%), paraparesis (10%), vertigo (8%), nausea and vomiting (8%), and cognitive disorder (5%).

3.1. Radiologic outcomes following GKRS

The mean follow-up time was 30.28±27.48 months (range 2-120 months). Six patients were followed for less than 6 months and one patient died in the fifth month of follow-up. The radiosurgery parameters of the patients are presented in table 1.

Total Patients Patients who Died Patients who Alive

Radiological Parameter

25.85±3.9424.9 ± 2.2 25.9 ± 4.0 Maximal dose (Gy)

13.21±1.9011.6 ± 1.3 13.3 ± 1.8 Marginal dose (Gy)

50.70±4.3946.6 ± 5.2 51.0 ± 4.1 Isodose (%)

99.06±1.0499 ± 1 99 ± 1.0 Tumor Coverage (%)

11.35±9.2018.1 ± 10.1

10.87 ± 9.0Tumor volume(cc)

Table 1: comparison of radiosurgical parameters in patients who lived or died during study

Radiological Parameter	**Patients who Alive**	**Patients who Died**	Total Patients
Maximal dose (Gy)	25.9 ± 4.0	24.9 ± 2.2	25.85±3.94
Marginal dose (Gy)	13.3 ± 1.8	11.6 ± 1.3	13.21±1.90
Isodose (%)	51.0 ± 4.1	46.6 ± 5.2	50.70±4.39

Tumor Coverage (%)	99 ± 1.0	99 ± 1	99.06±1.04
Tumor volume(cc)	10.87 ± 9.0	18.1± 10.1	11.35±9.20

Overall, five patients (8.2%) died. Of these patients, one was a woman and four were men, and two had a history of surgery, of whom one patient had three operations and another one had one operation. Radiologically increased tumor volume was seen in three patients who died because of tumor growth and its complications. There was no change in the tumor volume in two patients, of whom one suffered from an extensive stroke within five months and died, but the cause of death was not recorded for the other patient. Radiologic tumor control was achieved in 91.8% of patients, in whom the tumor volume decreased in 30 (49.2%) and remained unchanged in 26 (42.6%). An increase in tumor volume was noticed in five patients (8.2%), of whom three died and two were operated.

3.2. Clinical outcomes following GKRS

There was no significant difference in age at onset of symptoms between those who died and patients who survived. The age at diagnosis time was 61±18.76 years old in patients who died and 49.9±14.61 years old in patients who survived.

Eleven patients developed a refractory headache after GKRS due to evidence of brain edema, who all responded to corticosteroid therapy. There was a marked improvement in headache, nausea, vomiting, and vertigo in 56.9% of the patients (during 6 months' follow-up), while no change was seen in 35.3% of the patients. Five patients, who all had positive history of previous surgery, reported worsening of muscle weakness, headache, and vertigo. Two of these patients had three operations (one of these two had a history of radiotherapy following surgery), two had one operation, and one had history of radiotherapy followed by operation. Different radiologic tumor outcomes in last follow-up are shown in table 2.

3.3. Tumor outcomes and progression-free-survival

Table 2: The mean follow-up in patients with different radiological tumor outcomes

Radiologic tumors outcomes	Number of patients	Mean ± SD follow-up
Improved	30	34.47±31.90
No change	26	21.46±22.50
Progress	5	45.60±15.46

There was no significant difference between radiosurgical parameters and tumor volume in radiological tumor-related outcomes or clinical outcomes. gender did not correlate various tumor outcomes as well.

Mean ± SD follow-up Number of patients Radiologic tumors outcomes

31.90 ± 34.47 30 Improved

22.50 ± 21.46 26 No change

15.46±45.60 5 Progress

According to Kaplan-Meier analysis, the overall progression-free survival was 98.6% in 12 months, 96.9%±0.03% in 24 months, 92%±0.04% in 36 months, 86.6%±0.07% in 48 months, and 67.04%±13.4% in 60 months (Figure 1). There was no significant difference in progression-free survival between operated and non-operated groups.

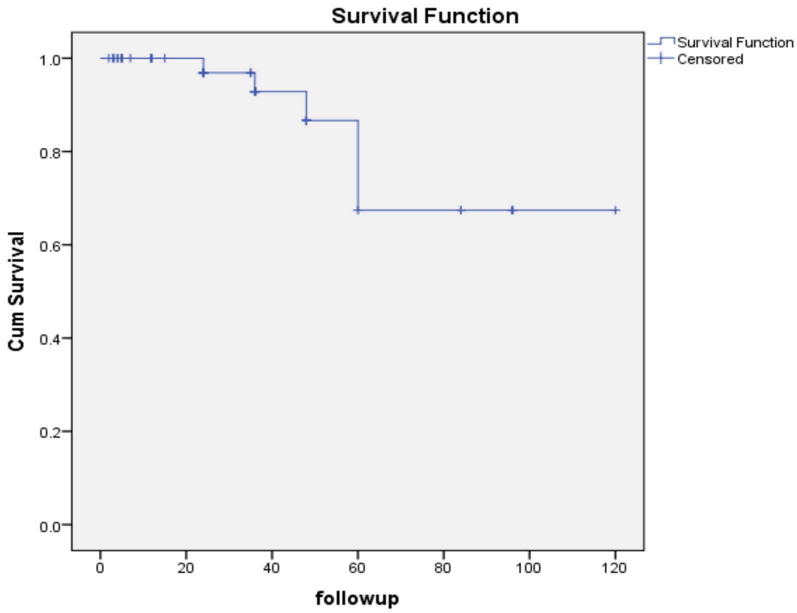

Fig.1. progression-free survival of all patients, follow-up time: 120 months

Discussion

While PSMs can involve critical adjacent structures such as the superior sagittal sinus and large cerebral veins, surgeons may encounter difficulties in management of these tumors. Therefore, the aim of treatment is not only removing the tumor mass but also controlling tumor (1, 6, 7). A bulk of studies in the literature have demonstrated that tumor resection surgery of PSMs is associated with a significant risk of recurrence (1, 6, 8-14). Recent investigations detected tumor recurrence in 27.2% of their cases during the mean follow-up time of 84.4 months (8). Raza and colleagues (6) reported an 11% recurrence rate after microsurgical resection in 61 patients with PSMs at a mean follow-up of 41 months. Moreover, Pettersson-Segerlind J et al. (10) reported long-term recurrence rate of 47% in 25-year-follow-up, and it increased with increasing Simpson grades. Despite these facts, radiosurgery showed more effectiveness in controlling PSMs (11, 15). Such studies were performed to evaluate the safety and efficacy of radiosurgery in PSMs' tumor control. They state that radiosurgery had no mortality and no risk of sinus thrombosis, as well (16). The 4% risk of headaches after radiosurgery was reported by Hadelsberg et al. (16); versus 32.8% of motor deficit after the operation which was most followed by headache, seizures, dysphasia , loss of vision and head tumescence, that was reported by Escribano Mesa et al.(8). It has been proved that radiosurgery had more advantages over open surgeries, with less harm to critical structures like arteries, veins and venous sinuses, at least at clinically performed radiation doses. Therefore, it can be an appropriate therapy when critical vessels are invaded by tumor mass and its cure by conventional surgery is accompanied with a high risk of sinus occlusion and trombosis (16).

In our investigations of 61 patients with diagnosis of PSM during 30.28 months follow-up time (range 2-120 months) after GKRS, the actuarial radiologic tumor control was 91.8%. This result was in concordance with the available literature. Seo et al.(17) reported the tumor control rate of 91.7% in 424 patients during 5 years. Another study performed by Hadelsberg et al. (16) on 74 patients showed parasagittal tumors which were controlled in 90.6% of patients at a mean follow-up time of 49 months. Hesagawa et al.(18) achieved the tumor control rate of 87% in 119 lesions including convexity, parasagittal, and falcine meningiomas, of which 49 lesions (41%) had regressed, 52 (44%) remained stable, and 18 (15%) had in-field tumor progression. We achieved nearly better results of tumor volume decreasing in 30 (49.2%) patients. This variable remained unchanged in 26 (42.6%) patients and increased in five patients (8.2%), of whom three died and two were operated.

Furthermore, we analyzed PFS using the Kaplan-Meier approach, as 98.6%, 92%±0.04%, and 67.04%±13.4% in 1-, 3-, and 5- years, respectively. PFS in a study performed by Sheehan et al. at 2, 3, and 5 years was 98%, 90%, and 90%, respectively (19). Hesagawa et al.(18) reported the actuarial 5- and 10- years PFS rate of 78% and 57%, respectively. There have been many investigations reported about predictors of PFS. Ding et al. have declared that the independent predictors of tumor PFS are tumor location (parasagittal), prior resection, and younger age (15). It is considerable that tumor volume, and margin dose were not associated with PFS (20), as we concluded in our study. Seo et al. (17) mentioned female sex and previous history of craniotomy as associated factors with tumor progression. However, we have found no association between history of surgery and PFS rate and no significant difference in sex, as well.

Although GKRS has more advantages in morbidities compared with surgery, we cannot fully protect neurovascular structures, particularly dural venous sinuses invaded by some of the tumors, from radiation exposure (21, 22). Moreover, studies have shown that the rate of stereotactic radiosurgery side effects is higher in non-basal regions, especially in the parasagittal region (4, 5). PSMs are at a particular risk for venous occlusive complication which leads to brain edema (2). The reason remains unclear, but seems to be caused by secretion of vasoactive substances in parasagittal region after radiosurgery (23). In our study, 56.9% of cases represented notably regression in their symptoms including headache, nausea, vomiting, and vertigo in 6 months of follow-up after administrating GKRS. Nevertheless, 11 (18.03%) patients developed a refractory headache due to evidence of brain edema, of whom all responded to corticosteroid therapy. It was justified in literature that gamma knife therapy could significantly improve symptoms like headache in new or recurrent cases of meningiomas (3). But, many studies declared that edema developed mostly in tumors around the critical structures such as midline and sagittal sinus, in comparison with skull based meningiomas (5, 20, 24-26). It seems that PSMs are more likely to be radio-resistant than other meningiomas and trend to present edema following radiosurgery, as well (18, 27, 28).

In a study by Sheehan and colleagues on 61 patients with median follow-up time of 28 months, edema progression after GKRS in 77 parasagittal and parafalcine tumors were reported in 40% of tumors, of which 26% regressed in time. Also 25% represented regression and 23% remained stable brain edema, respectively (19). A multivariate analysis performed recently has indicated anatomical location of tumor and its invasion to venous sinus (parasagittal location), tumor volume, margin, and maximal dose in radiosurgery administration as well as history of pretreatment edema, and sagittal sinus occlusion, as potential factors associated with post-radiosurgical edema (26, 28). One study has demonstrated that tumors accompanied by preexisting edema were more likely to present progressive edema after administrating radiosurgery, and no prior resection was related to occurrence of new or worsening edema, as well (19). Furthermore, Kollova et al. found that a margin dose greater than 16 Gy was a risk factor associated with edema (3). However, we found no considerable association between radiologic findings (most notably edema) and radiosurgical parameters such as maximum dose delivery, marginal dose and isodose as well as tumor volume. Moreover, in our investigation five patients who all had positive history of previous surgery, reported worsening of muscle weakness, headache, and vertigo. Two of these patients had three operations (one of these two had a history of radiotherapy following surgery), two had one operation, and one had history of radiotherapy followed by operation. There was no change in 35.3% of the patients.

Hesagawa et al. found that initial treatment by Gamma knife can expose patients with peritumoral edema particularly at first 3 months after radiosurgery. They reported edema rate of 50% (21 of 42 patients) in a group with initial treatment of Gamma knife in compared with 13% (8 of 61) peritumoral edema occurrence of whom had previous surgery(18). Our data showed that of those 11 patients whom represented edema, only 4 patients had history of at least one resection surgery before and 7 patients underwent initial treatment of GKRS. Consequently, stereotactic radiosurgery is truly potential to control tumor growth by itself, though it seems to be effective still as an adjuvant therapy due to the risk of progressive peritumoral edema, particularly in PSMs.

As limitations of this study, we did not evaluate the patients' endocrine function and the follow-up time was not long enough. Investigation of these parameters in other studies with larger sample sizes may provide an accurate assessment of GKRS's effects PSMs.

Conclusions

In conclusion, GKRS is a safe and effective choice as first or second lines of treatment of parasagittal meningiomas.
In conclusion, GKRS is a safe and effective choice as first or second lines of treatment of parasagittal meningiomas.
We did not find any association between patient age and tumor size and radiosurgery parameters as potential factors with edema following radiosurgery.

Considering the critical location of parasagittal tumors, combined treatment approach of radiosurgery with microsurgery may facilitate following complications, particularly conditions in which the tumor has completely invaded within the superior sagittal sinus and total resection accompanied with high risk of mortality.

because radiosurgery management in PSMs encounter such limitations, we suggest long-term follow-up to diagnose life-threatening complications including brain edema.

Disclosure of interest

The authors declare that they have no competing interest.

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