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ORIGINAL ARTICLE

Intracranial meningioma: Experience with stereotactic radiotherapy

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Summary

Purpose: *Definitive radiotherapy is a treatment option for patients with inoperable meningiomas. The purpose of this study was to evaluate the results of stereotactic radiotherapy as first-line treatment for intracranial meningiomas that were diagnosed radiologically.*

Methods: *Between January 2010 and June 2016, 56 patients with intracranial meningioma treated with Cyberknife-based Stereotactic Radiosurgery (SRS) or hypofractionated stereotactic radiotherapy (hFSRT) were included. The median prescribed radiation dose was 16 Gy (range 13-18) for SRS and 25 Gy (range 18-33) for hFSRT. hFSRT doses were delivered in 3 to 5 fractions.*

Results: *Median follow-up was 58 months (range 6-97). Overall survival (OS) for the whole group was 89.2%; for SRS group it was 100% and for hFSRT group 87.5% (p=0.29). Progression free survival (PFS) for the whole group was 89.3%; for SRS group it was 87.5% and for hFSRT 89.5% at 5 years (p=0.93).*

Conclusion: *SRS and hFSRT were effective with excellent local control rates and they can be an alternative treatment option for patients with inoperable meningiomas.*

Key words: *cyberknife, fractionated stereotactic radiotherapy, meningiomas, stereotactic radiosurgery*

Introduction

Intracranial meningiomas are the second most frequent primary brain tumors, representing 20% of all intracranial tumors. They arise from the cap cells of the arachnoid membrane and occur more frequently in women than in men [1,2]. A high percentage of meningiomas present as small, slow growing, asymptomatic tumors without brain edema. However,without treatment they may progress locally, compressing adjacent structures and causing neurologic deficits.

The World Health Organization (WHO) histological grading classification is the most commonly used, with benign, atypical, and malignant (anaplastic) meningiomas classified as WHO grade I, II, and III, respectively [3]. Ninety percent of meningiomas are benign, and WHO grade II and III tumors occur approximately in 10% and 2%, respectively [4-9].

Surgical resection of the entire tumor, when possible without neurologic injury, is the standard of care, but may be limited by the size and the location of the tumor [2-9].

More recent experience suggests stereotactic radiotherapy as a primary treatment for well-selected meningiomas [10-12]. Stereotactic radiotherapy demonstrated excellent results, equivalent

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local control to both conventional radiation therapy and surgical resection for select groups of meningioma patients [10,11].

We retrospectively analyzed the patients with meningioma who were treated with stereotactic radiotherapy using a robotic, frameless device (CyberKnife, Accuray Inc, Sunnyvale, CA, USA). In this monocentric study, we analyzed the clinical outcomes, including tumor control and survival, to evaluate the results of stereotactic radiotherapy for this particular patient group.

Methods

Patients

A retrospective analysis was carried out in 56 patients with intracranial benign meningiomas treated with CyberKnife SRS from January 2010 to June 2016 at Ankara Oncology Training and Research Hospital, Radiation Oncology Department. Patients who had undergone stereotactic radiotherapy for intracranial meningiomas were included in the present study. None of them had undergone biopsy or surgery for their tumors. All patients were diagnosed radiologically and were evaluated by MRI before treatment.

Thirty-two female and 24 male patients were included. Their median age was 56 years (range 31-78). Eight patients underwent SRS while 48 underwent hFSRT. All diagnoses were radiological. The median tumor volume of SRS group was smaller than hFSRT group (6.8 cc and 7.5 cc, respectively). Patient characteristics, site of lesions and fractionation schedules are summarized in Table 1.

Table 1. Patient and treatment characteristics

Characteristics	*n (%)*
Age, median (range)	56 (31-78)
Gender	
Female	32 (57)
Male	24 (43)
KPS	
60	1 (2)
70	4 (7)
80	11 (21)
90	40 (70)
Location	
Supratentorium	37 (64)
Infratentorium	19 (33)
Total tumor volume, cc (range)	7 (0.4-23.5)
Follow-up time, months (range)	62 (6-321)
SRS	
No. of patients	8 (14)
Tumor volume, cc (range)	6.8 (0.6-9.9)
Dose, Gy (range)	16 Gy (13-18)
hFSRT	
No. of patients	48 (86)
Tumor volume, cc (range)	7.5 (0.4-23.5)
Sessions	
3	13 (23)
5	35 (63)

Treatment

A high resolution thin-slice (1 mm) CT scan and magnetic resonance imaging (MRI) scan were performed and fused to the planning CT scan to improve target identification.The gross tumor volume (GTV) was defined as tumor on T1 contrast-enhanced MRI. Planning target volume (PTV) was created by adding 1mm margin to GTV. The radiosurgery dose was prescribed to cover the PTV. The prescribed dose and fractionation schedule were determined by the treating radiation oncologist and considered according to the size of the lesion and proximity to nearby critical structures [13]. hFSRT was applied using either 3 fractions (range 18-25 Gy) or 5 fractions (range 20-33 Gy) prescribed to the median 89% isodose line (range 80-98%). For SRS a single dose of 13-18 Gy was prescribed. In most cases, the dose was prescribed to the isodose surface that encompassed the margin of the tumor. The median tumor volumes were 6.8 cc (range 0.6-9.9) for SRS and 7.5 cc (range 0.4-23.5) for hFSRT.

Treatment plans were generated in the CyberKnife nonisocentric inverse treatment planning software (Multiplan, Accuray).

Follow-up

Median follow-up was 58 months (range 6-97). MRI was repeated at 3-month intervals during the first year following SRS and every 4 to 6 months thereafter. Brain MRI results were used to score local and regional failures. Local failure was defined as progression of the treated lesion (ie, enlargement of existing tumor). Regression was defined as tumor shrinkage of ≥2 mm in diameter, and progression as ≥2 mm enlargement.

Statistics

For data analysis the statistical software SPSS for Windows (version 24.0) was used. The Kaplan–Meier method was used to calculate OS and PFS. OS was calculated from the first day of radiotherapy until death. A result was significant if $p<0.05$. When calculating the PFS rate, the dates of imaging follow-up examinations were used. Increases and reductions of >2 mm in the longest diameter of the tumor were considered to represent tumor progression and regression, respectively. Tumors whose diameters changed by <2 mm were labeled as stable.

Results

The median follow-up was 58 months (range 6-144) and all patients were followed-for at least 6 months.The median target volume was 7 cc (range 0,4-23,5; median 6.8 cc for SRS and 7.5 cc for hFSRT).

OS for the whole group was 89.2%; for SRS group it was 100% and for hFSRT group 87.5% (Figure 1). All deaths resulted from other diseases.

PFS for the whole group was 89.3% at 5 years (Figure 2); for the SRS group it was 87.5% at 5 years and for the hFSRT group 89.5% (Figure 3).

The effect of tumor volume on treatment response was also evaluated. The 5-year PFS rate was 79.1% for the 24 patients with tumor volume ≥8 cc and 96.8% for the 32 patients with tumor volume <8 cc (p=0.031, Figure 4).

Stable disease based on MRI was seen in 36 patients, while 14 patients had a reduction of tumor volume and 6 patients had progression. Table 2 shows the tumor response rates. All patients with progression were refered for surgery.

Discussion

Surgery is the preferred treatment for intracranial meningiomas but sometimes complete resection without significant morbidity is difficult to achieve due to the location of the tumor. Definitive radiotherapy can be an effective treatment for inoperable meningiomas.

Table 2. Tumor response

	Progression *n*	*Stable* *n*	*Regression* *n*	*Total*
SRS	1	5	2	8
hFSRT	5	31	12	48
Total, n (%)	6 (10.7)	36 (64.3)	14 (25)	56 (100)

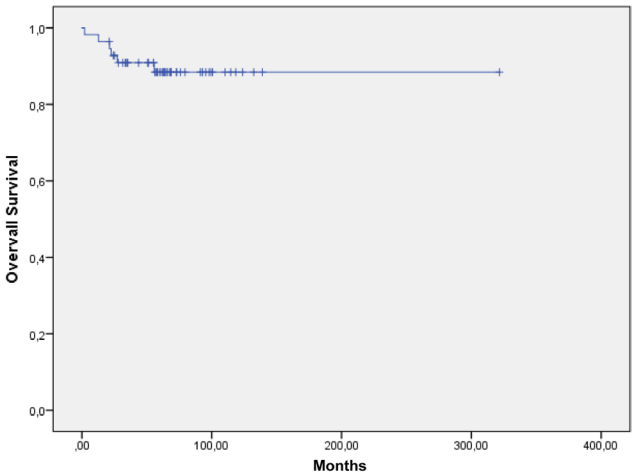

Figure 1. Overall survival of the whole group.

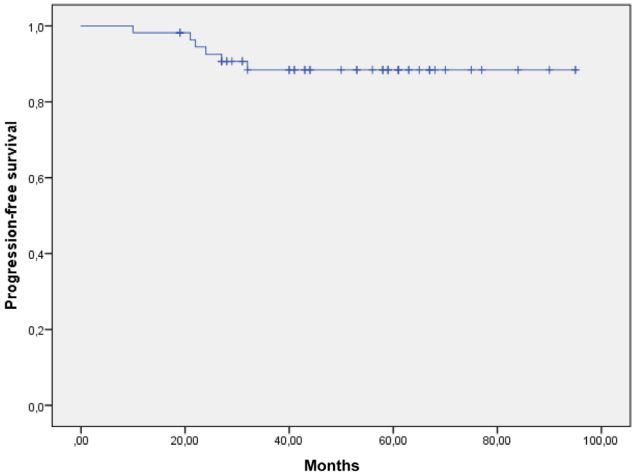

Figure 2. Progression free survival of the whole group.

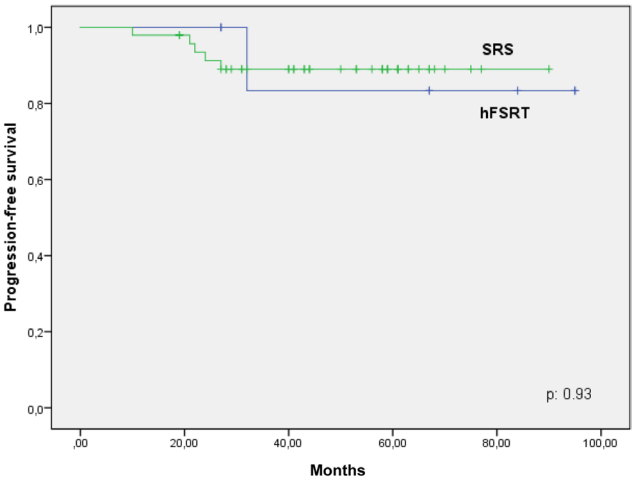

Figure 3. Progression-free survival for SRS and hFSRT group.

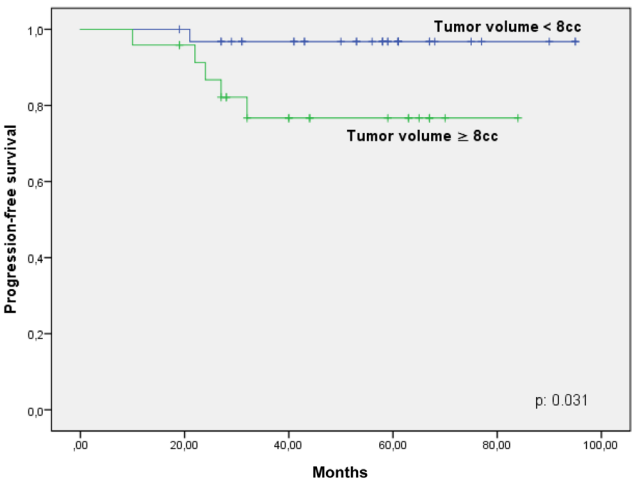

Figure 4. Progression-free survival rates for patients with tumor volume <8 cc and ≥8cc.

In this single-institution study, we reviewed data obtained from patients with meningioma treated by stereotactic radiotherapy. Stereotactic radiotherapy/radiosurgery was considered in the following cases: (1) patients with unresectable meningiomas; (2) patients with meningiomas in high-risk functional areas; (3) patients with decreased performance status for surgery or patients that refuse surgery.

Previous studies reported 86-100% tumor control rates for intracranial meningiomas treated with streotactic radiotherapy [14,15]. Kondziolka et al. reported a tumor control rate of 95% . In the Mayo clinic study a tumor control rate of 99% was reported at 7 years. Eklebawy et al. reported 94% PFS rate for 32 patients at 5 years. Debus et al. Followed-up 189 patients who were treated with stereotactic radiotherapy; only 3 patients recurred. In our study, PFS for the whole group was 89.3% at 5 years and tumor progression was 10.7%; these data are comparable with other reports.

Considering tumor location, poorer local control rates were observed in patients with falx lesions with respect to other locations. In their study Solda et al. [17] included only grade I meningiomas and reported similar findings that falx/convexity located tumors had more aggressive characteristics. In this study we found no relationship between the local control rate and tumor location but we did not evaluate the tumor location details. Our evaluation included only the infratentorial or supratentorial location; this undetailed classification could be the reason of finding no relationship between local control rates and tumor localization.

In this study, it was found that large tumors (≥8 cc) had poorer PFS rates. Similar results have been reported for large tumors [18,19].

The limitations of this study include the definition of tumor response and the method of diagnosis. We defined regression as 2 mm shrinkage in tumor diameter, but while measuring the tumor diameter it is really difficult to overlay the same slices. So the comparison may not be exact enough. Using the tumor volume shrinkage/enlargement may be more proper than the tumor diameter.

All the tumors in this study were imaging-diagnosed and not confirmed histologically. If the patients had undergone biopsy or surgery, some of them could be reported as atypical meningioma. It is difficult to distinguish malignant gliomas from benign types. D-thallium-201 chloride single-photon emission CT and diffusion MRI may be useful to distinguish these two conditions, but of course these imaging methods are not sufficient for definitive diagnosis. Further investigations are needed on this topic.

In conclusion, this study demonstrated the efficacy of stereotactic radiotherapy in patients with inoperable meningioma. Radiotherapy may be considered as a safe and effective treatment method in this patient group.

Conflict of interests

The authors declare no conflict of interests.

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