JOURNAL OF
CONTEMPORARY MEDICINE

DOI:10.16899/jcm.1256587
J Contemp Med 2023;13(3):426-432

Original Article / Orijinal Araştırma

Outcomes of Meningioma Patients Undergoing Stereotactic Radiotherapy

Stereotaktik Radyoterapi Uygulanan Menengiom Tanılı Olgularda Tedavi Sonuçlarımız

Ela Delikgoz Soykut[1], Dönay Aksan[1], Evrim Şavlı[1], Salih Buğra Yılmaz[2], Hatice Tataroğlu[1]

[1]Samsun Training and Research Hospital, Department of Radiation Oncology, Samsun, Turkey
[2]Samsun Training and Research Hospital, Department of Neurosurgery, Samsun, Turkey

Abstract

Aim: Innovations in radiotherapy have paved the way for alternative approaches for the treatment of meningioma, and in this context, radiosurgery has begun to be used in the treatment of meningioma. This study aimed to examine the clinical results of radiosurgery in the treatment of meningioma and to show whether it achieves the main goals, especially in terms of the possibility of tumor control and the success of preventing progression.

Material and Method: Primary, residual, and recurrent meningioma treated with stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT) between 2013 and 2020 were evaluated retrospectively. Study endpoints were overall survival (OS), progression free survival (PFS), and local control (LC).

Results: 73 patients and 81 lesions were analyzed. The median duration of the follow-up period was 49 months (range, 7–138 months). 5- and 7-y OS and PFS were 87.6%, 78.9%; 82.9% and 82.9%, respectively. The tumor control rate was 94.6%. In univariate analysis, gender (p=0.007), radiosurgery for recurrence (p=0.011) and number of lesions (p=0.030) were found to be factors affecting OS, and number of lesions (p<0.001), grade (p=0.048) and tumor size (p=0.047) were found to be factors affecting PFS. Number of lesions (p=0.022) was remained prognostic factor for PFS in the multivariate analysis.

Conclusion: Since SRS/SRT can provide high tumor control in the management of meningioma, it can be preferred as an alternative treatment method, especially in patients who are diagnosed radiologically, who are not candidates for surgery or who refuse surgical treatment, as well as in cases of residual and recurrence in the post-surgical period.

Keywords: Meningioma, stereotactic radiosurgery, stereotactic radiotherapy

Öz

Amaç: Radyoterapideki yenilikler menengiom tedavisinde alternatif yaklaşımların önünü açmış ve bu bağlamda radyocerrahi menengiom tedavisinde kullanılmaya başlanmıştır. Bu çalışma, radyocerrahinin menengiom tedavisinde klinik sonuçlarını incelemek ve özellikle tümör kontrolü olasılığı ve ilerlemeyi önleme başarısı açısından ana hedeflere ulaşıp ulaşmadığını göstermeyi amaçladı.

Gereç ve Yöntem: 2013-2020 yılları arasında stereotaktik radyocerrahi (SRC) ve stereotaktik radyoterapi (SRT) ile tedavi edilen primer, rezidüel ve nüks menengiomlar retrospektif olarak değerlendirildi. Çalışma son noktaları, genel sağkalım (GS), progresyonsuz sağkalım (PS) ve lokal kontrol (LK) idi.

Bulgular: 73 hasta ve 81 lezyon analiz edildi. Medyan takip süresi 49 aydı (aralık, 7-138 ay). 5- ve 7-y GS ve PS sırasıyla %87,6, %78,9; ve %82,9, %82,9'du. Tümör kontrol oranı %94,6'ydı. Tek değişkenli analizde cinsiyet (p=0,007), nüks nedeniyle radyocerrahi (p=0,011) ve lezyon sayısı (p=0,030) GS'ı etkileyen faktörler olarak bulundu ve lezyon sayısı (p<0,001), grad (p= 0,048) ve tümör boyutu (p=0,047) PS'ı etkileyen faktörler olarak bulundu. Çok değişkenli analizde lezyon sayısı (p=0,022) PS için prognostik faktör olarak kaldı.

Sonuç: SRC/SRT menengiom tedavisinde yüksek tümör kontrolü sağlayabildiği için özellikle radyolojik olarak tanı konulan, cerrahiye aday olmayan veya cerrahi tedaviyi reddeden hastalarda, aynı zamanda ameliyat sonrası dönemde rezidüel ve nüks durumlarında alternatif bir tedavi yöntemi olarak tercih edilebilir.

Anahtar Kelimeler: Menengiom, stereotaktik radyocerrahi, stereotaktik radyoterapi

Corresponding *(İletişim)*: Ela Delikgoz Soykut, Samsun Training and Research Hospital, Department of Radiation Oncology, Samsun, Turkey
E-mail *(E-posta)*: eladelikgoz@gmail.com
Received *(Geliş Tarihi)*: 01.03.2023 **Accepted *(Kabul Tarihi)*:** 02.04.2023

INTRODUCTION

Today, the prevalence of meningioma diagnosis has increased with the prolongation of life expectancy and the more frequent and easier access to imaging techniques.[1] Since they have a slow growth pattern, they are usually asymptomatic unless they are adjacent to the critical structure and are detected incidentally without any neurological findings. The presence of symptoms, the location and size of the tumor, as well as the patient's preference are the factors that should be considered in the management of meningioma.[2,3] While incidentally detected, asymptomatic, small lesions can be followed, radical surgery is often preferred for large lesions or for symptomatic relief in cases with neurological findings.[3] However, surgery is not appropriate in eloquent areas due to the increased risk of cranial nerve deficit or vascular damage. Radiosurgery can be applied as an alternative to surgery in patients for whom surgery is not suitable or depending on the patient's request.

The innovations in radiotherapy opened alternative approaches for the treatment of meningioma. Radiosurgery has been used in the treatment of meningioma for about 30 years.[4] There is no randomized study comparing surgery and radiosurgery yet, but results from radiosurgery studies including large series confirm that radiosurgery can be an alternative to surgery. In a retrospective study comparing radical surgery and radiosurgery in small meningiomas, local control was shown to be similar.[5] Radiosurgery in benign meningiomas has been shown to provide local control (LC) rates ranging from 85-97% in 5 years in many large series.[6-8] In addition, adjuvant radiosurgery following subtotal excision of benign meningiomas has yielded satisfactory results.[9] Radiosurgery is often added to surgery as a combined treatment in skull base meningiomas where gross total excision is not possible.[10] Finally, radiosurgery is applied in recurrent disease.[3]

Currently, radiosurgery is applied in the treatment of meningioma with the indications mentioned above, so in this study, we aimed to examine the clinical outcomes of radiosurgery in the treatment of meningioma and to show whether it achieves the main goals, particularly in terms of the possibility of tumor control and the success of preventing progression.

MATERIAL AND METHOD

Patient Selection and Data Collection

For this single-center retrospective analysis, all consecutive cases of primary, residual, and recurrent intracranial meningioma treated with stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT) between October 2013 and December 2020 were evaluated. Patients with a histologically or radiologically confirmed diagnosis and patients older than 18 years of age were included. Patients who received more than 5 fractions were excluded from the study. Patient charts were reviewed and demographic information of patients, tumor and treatment characteristics, clinical outcomes and treatment-induced adverse events are all reported. The study was conducted in accordance with the Declaration of Helsinki and was approved by the medical ethics committee of our institute. Individual approval was waived due to retrospective design. The study was approved by The University of Health Sciences, Samsun Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (No:2021/12/3, Date:23.6.2021)

Treatment Planning

CyberKnife® (Accuray, Sunnyvale, USA) Robotic Radiosurgery System was used in radiosurgery technique. For treatment planning, the software Multiplan v4.5 and 6D Skull Tracking system were used for treatment planning and delivery. Simulation computed tomography was performed with a slice thickness of 1 mm. A custom-made aquaplast mask was used for immobilization. Target structures were contoured after image fusion with T1-weighted magnetic resonance image with gadolinium contrast. The gross tumor volume (GTV) was defined as contrast-enhanced mass. The planning target volume was obtained by adding 1 mm to the GTV in 7 patients, otherwise it was the same as the GTV. Treatment was administered in single or multiple fractions depending on target volume and proximity to critical structures.

Follow-up

The patients were followed up regularly both clinically and radiologically. All patients were seen 1-3 months after treatment to assess the presence of symptoms associated with acute toxicity. Symptom control was recorded as clinical improvement or stability and no new complaints after SRS/SRT. Serial radiological evaluations were performed at 6-month intervals in all patients after the first imaging was performed 3 or 6 months after treatment.

Tumor responses were evaluated radiologically during the follow-up period. Local failure was defined as tumor growth greater than 2 mm in at least one of the tumor diameters. Distant failure was defined as a new lesion outside the initial treatment region. LC was defined as a stable response and/or partial response with tumor shrinkage.

Endpoints and Statistical Analysis

Study endpoints were overall survival (OS), progression free survival (PFS), and LC. OS was defined as the time elapsed between the date of treatment to the date of death or lost to follow-up. PFS was calculated as the time elapsed between the date of treatment to the date of radiographic evidence of a new lesion outside the SRT field or the date of radiographic evidence of local failure or the date of death. LC was defined as the absence of local tumor progression including all cases of stable response.

Continuous variables are expressed as the medians. Categorical variables are expressed as the frequency and percentage (%). The Kaplan-Meier method was used to estimate time-related censored endpoints. The differences were compared using log-rank statistics. Factors affecting survival were analyzed by Cox's proportional hazards model. All statistical analyses were performed using SPSS 25.0 statistical software (IBM Corp., Armonk, NY, USA). A p-value < 0.05 was considered as statistically significant.

RESULTS

Data from 73 patients and 81 lesions meeting the inclusion criteria were analyzed. All characteristics of the patients are reported in **Table 1**. Thirty-two of the patients were radiologically compatible with grade 1 meningioma. Forty-four of the patients had undergone previous surgery, pathologically 23 patients were grade 1 and 18 patients were grade 2 meningiomas. After surgery, 18 of them underwent SRS/SRT because of residual disease, while 23 of them underwent SRS/SRT because of recurrence. Forty-six patients were symptomatic and the most common findings were headache and motor loss. The most common localizations were skull base, falx and convexity. The median tumor size was 25 mm (9-59), and the median tumor volume was 6.92 cc (0.7-31.30) 9.92 (0.7-31.30). A median of 12 (12-18) Gy was performed in single fraction, and a median of 18 (18-25) Gy was performed with a median of 3 (2-5) fractions. The median prescription isodose was 83% (77-88).

The median duration of the follow-up period was 49 months (range, 7–138 months). At the end of the follow-up period, 8 patients died, 4 of which were tumor-related deaths. OS had a mean value of 80.06 (95% CI 73.66–86.47) months, median OS could not be achieved (**Figure 1a**). 5- and 7-y OS were 87.6% and 78.9%, respectively. In univariate analysis, gender (p=0.007), number of lesions (p=0.030), and radiosurgery for recurrence (p=0.011) were found to be factors affecting OS (**Figure 1b, 1c, 1d**). In patients with radiosurgery performed for recurrence, 5-y OS was lower than those performed for residual disease and image-diagnosed meningioma (68.3% vs 100% vs 95.2%). 5-y OS were 83.7% and 78.8% for grade 1 and grade 2. Age, location, grade, tumor size, and SRS/SRT were not associated with OS (**Table 2**).

Local recurrence observed in 4 patients and new lesions observed in 2 patients. PFS had a mean value of 81.33 (95% CI 74.73–87.93) months, median PFS could not be achieved (**Figure 2a**). 5- and 7-y PFS were 82.9% and 82.9%, respectively. In univariate analysis, number of lesions (p<0.001), grade (p=0.048) and tumor size (p=0.047) were found to be factors affecting PFS (**Figure 2b, 2c, 2d**). Age, gender, location, and SRS/SRT were not associated with PFS. However, mean PFS was lower in patients who underwent radiosurgery for recurrence than those who underwent primary and residual, but it was not statistically significant (61.51 vs 80.27 vs 85.62 months, p=0.173). In 41 meningiomas of known grade, the 5-y PFS rate was 92.3% in grade 1 meningiomas and 57.9% in grade 2 meningiomas, a statistically significant difference was found (p=0.048). 5-y PFS was found to be 100% in cases with a tumor diameter less than 2 cm, and 71.9% in cases with a tumor diameter greater than 2 cm (p=0.047). Number of lesions (p=0.022) was remained prognostic factor for PFS in the multivariate analysis (**Table 2**).

The tumor control rate was 94.6%. The tumor volume decreased after SRT in 20 patients, remained stable in 49 patients. Tumor progression occurred in 4 patients (5.4%) at a median of 42 months (12-55 months). Response was obtained in the treated lesion in 2 patients, while new lesions were detected outside the initial SRS/SRT area. SRS/SRT was applied to 1 of the newly detected lesions, surgery was performed to the other and 3 of the progressive lesions, and 1 lesion was being followed up. At the last control, it was found that the symptoms were absent or decreased in 17 patients, similar in 21 patients, and worsened in 7 patients.

Table 1. Clinicopathological and Treatment Characteristics

Variable	N (%)	Median (range)
Age		60 (32-87)
Gender		
Female	50 (68.5)	
Male	23 (31.5)	
Location		
Skull base	23 (28.1)	
Falx	17 (20.7)	
Convexity	16 (19.5)	
Others	25 (31.7)	
Symptoms*		
Headache	21 (28.3)	
Motor loss	15 (20.5)	
Visual loss	10 (13.7)	
Hearing loss	2 (2.7)	
Epilepsy	2 (2.7)	
Asymptomatic	26 (35.6)	
Diagnosis		
Image-diagnosed	40 (49.3)	
Pathologically-diagnosed	41 (50.7)	
Pathology		
Grade 1	23 (56.1)	
Grade 2	18 (43.9)	
Number of lesions		
1	60 (82.2)	
>1	13 (17.8)	
Radiosurgery indication		
Primary (Image-diagnosed)	40 (49.3)	
Residue	18 (22.2)	
Recurrence	23 (28.5)	
Size of tumor (cm)		2.5 (0.9-5.9)
Volume of tumor (cc)		9.92 (0.7-31.30)
RT dose (Gy)		
SRS	34 (41.5)	12 (12-18)
SRT	48 (48.5)	18 (18-25)
RT fraction		
1	34 (41.5)	1
>1	48 (48.5)	3 (2-5)
Prescribed isodose		83 (77–88)

RT: Radiotherapy; SRS: Stereotactic radiosurgery; SRT: Stereotactic radiotherapy
* Some symptoms were observed together.

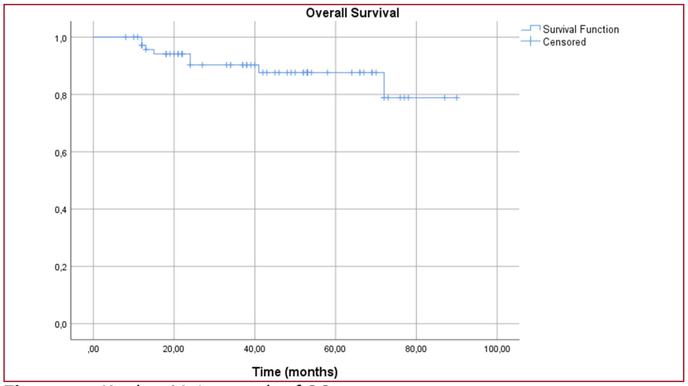

Figure 1a. Kaplan-Meier graph of OS.

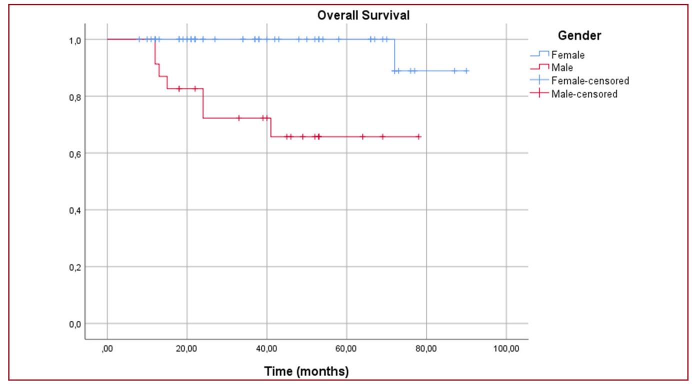

Figure 1b. Kaplan-Meier graph of OS according to gender.

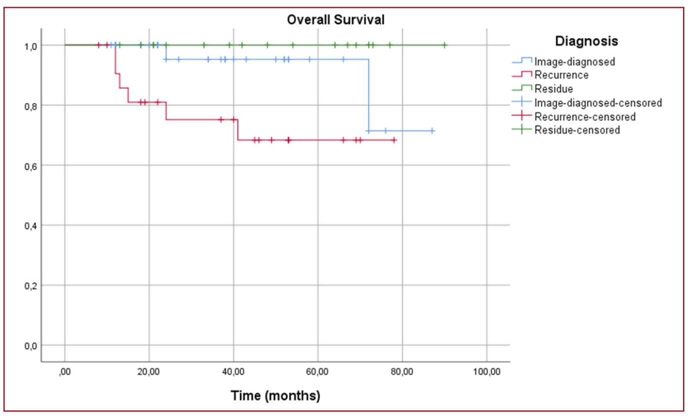

Figure 1c. Kaplan-Meier graph of OS according to diagnosis.

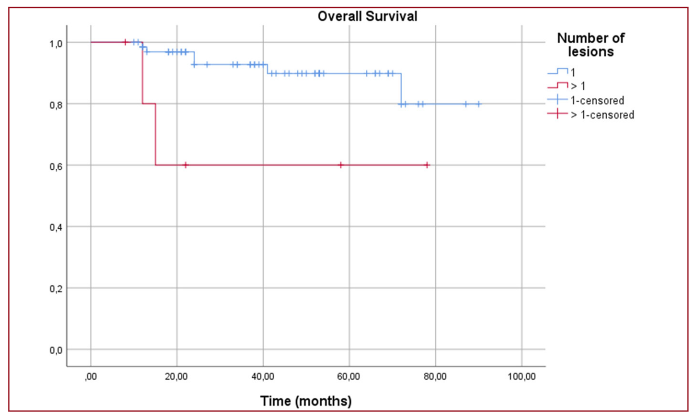

Figure 1d. Kaplan-Meier graph of OS according to number of lesions.

Table 2. Survival Outcomes

Factors	OS				PFS			
	Univariate Analysis				Univariate Analysis			
	Mean	HR (CI 95%)	5-y	p	Mean	HR (CI 95%)	5-y	p
Age								
≤60	83.60	3.44(76.86-90.34)	92.7	0.423	79.88	4.58(70.89-88.80)	78	0.238
>60	63.47	3.90(55.81-71.13)	82.7		69.08	2.69(63.81-74.35)	93.5	
Gender								
Female	88.00	1.88(84.30-96.69)	100	0.007	83.39	3.59(76.35-90.43)	85.6	0.129
Male	58.68	6.03(46.85-70.52)	65.7		66.23	4.12(53.16-69.31)	80.5	
Location								
Skull base	77.75	4.85(68.24-87.27)	90.4		-		100	
Falx	86.50	3.37(79.89-93.11)	92.9	0.511	-		67.9	0.204
Convexity	60.96	7.06(47.12-74.80)	78.6		-		83.9	
Others	57.00	5.80(45.61-68.38)	83.3		-		85.7	
Radiosurgery indication								
Image-diagnosed	-		95.2	0.011	80.27	4.50(71.44-89.39)	87.3	0.173
Residue	-		100		85.62	4.09(77.60-93.64)	87.5	
Recurrence	-		68.3		61.51	4.48(52.71-70.30)	79.7	
Grade								
Grade 1	69.09	4.11(61.03-77.16)	83.7	0.781	70.76	2.14(66.56-74.97)	92.3	0.048
Grade 2	74.77	9.59(55.97-93.57)	78.8		65.67	11.41(43.30-88.04)	57.9	
Tumor size								
<2 cm	78.84	4.83(69.36-88.32)	92.3	0.577	-		100	0.047
≥2 cm	79.37	4.05(71.43-87.31)	85.3		-		71.9	
Number of lesions								
1	81.62	3.20(75.33-87.91)	89.8	0.030	83.85	3.01(77.94-89.76)	87.6	<0.001
>1	52.20	14.13(24.49-79.91)	60		34.00	10.00(14.40-53.60)	0	
Radiotherapy								
SRS	63.74	4.38(55.15-72.32)	80	0.748	69.68	2.27(65.25-74.13)	96	0.418
SRT	80.96	3.78(73.49-88.31)	90.2		79.50	4.32(71.00-87.97)	78.6	
	Multivariate Analysis				Multivariate Analysis			
Gender		7.61(0.94-102)		0.054		-		-
Radiosurgery indication		4.25(0.79-22.80)		0.091		-		-
Grade		-		-		7.99(0.81-78.43)		0.074
Tumor size		-		-		16.46(0.05-422.1)		0.269
Number of lesions		1.89(0.31-11.62)		0.488		8.22(1.34-53.12)		0.022

CI: Confidence interval; HR: Hazard ratio; OS: Overall survival; PFS: Progression free survival; SRS: Stereotactic radiosurgery; SRT: Stereotactic radiotherapy

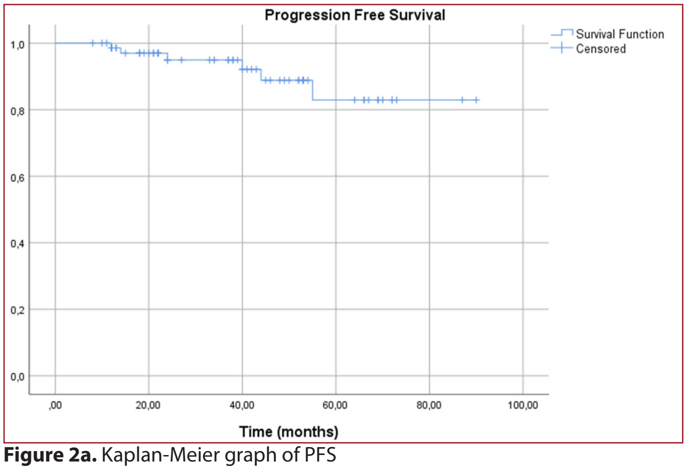

Figure 2a. Kaplan-Meier graph of PFS

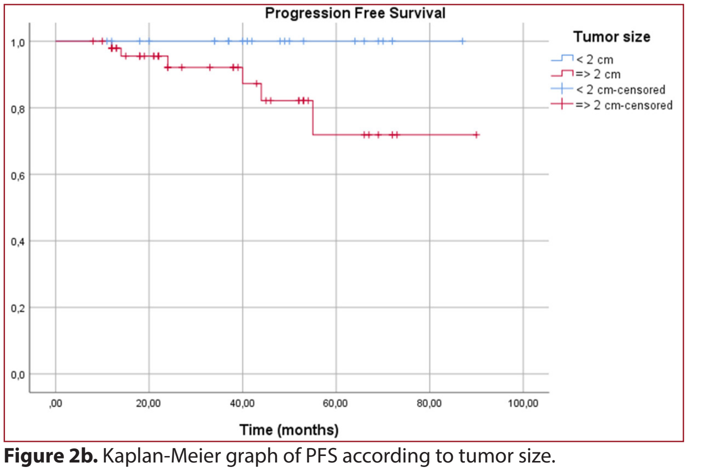

Figure 2b. Kaplan-Meier graph of PFS according to tumor size.

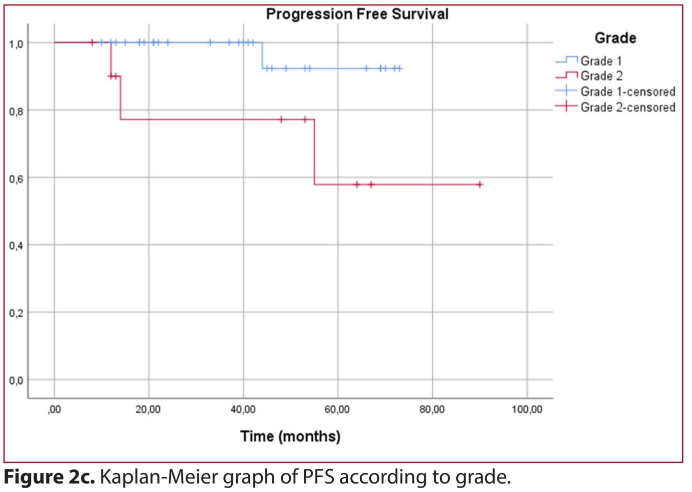

Figure 2c. Kaplan-Meier graph of PFS according to grade.

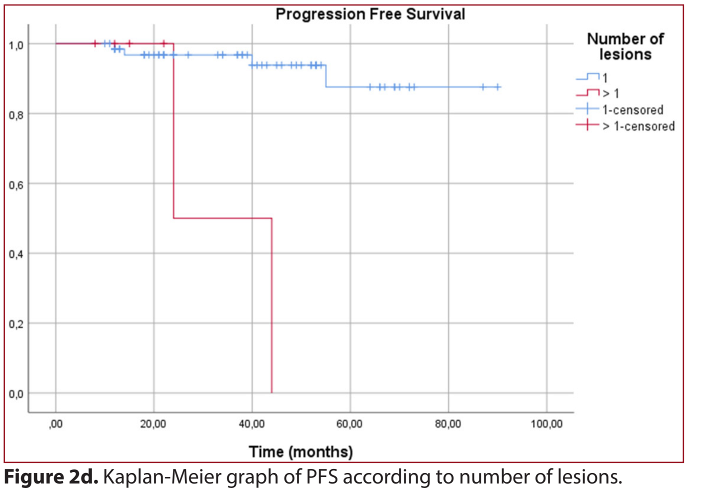

Figure 2d. Kaplan-Meier graph of PFS according to number of lesions.

DISCUSSION

The present analysis aimed to examine the clinical outcomes of SRS/SRT in the treatment of meningioma and to show whether it achieves the main goals, particularly in terms of the possibility of tumor control and the success of preventing progression. It is also aimed to identify factors that may affect clinical outcomes. At a median follow-up of 49 months, we found 5- and 7-y results similar to those in the literature.[5-10] In univariate analysis, it was shown that increasing tumor size and grade negatively affected PFS, radiosurgery due to recurrence adversely affected OS, and increased lesion number negatively affected both.

Previous studies including large series have shown that radiosurgery in benign meningiomas yields LC rates ranging from 85-97% at 5 years.[5-11] In some series with 10-y results, this rate was reported to be between 69-92%.[6-8,11,12] In our study, we found 7-y LC over 94%, we can report that our results are consistent when compared with the results obtained from the literature.

SRS/SRT has long been involved in the treatment of meningiomas. Although the available data are mostly retrospective data, they are considered safe with long follow-up periods. When the studies are examined, it is seen that there is a homogeneous patient population selected according to the diagnosis, surgical status and location, as well as studies belonging to heterogeneous groups in which various parameters are combined. Our study was highly heterogeneous as it included patients with image-diagnosed meningioma who underwent radiosurgery, as well as patients who underwent radiosurgery for post-operative residual or recurrent disease. In 2014, Kondziolka et al.[7] reported that there was no difference in terms of LC and PFS in 290 meningioma cases, of which almost half had undergone previous surgery. In their study, 22 of the patients underwent SRS for relapse and 114 for residual disease. The authors did not report a difference in OS in relapsed patients, but in our study, worsened OS was detected in patients who underwent SRS/SRT for relapse. In addition, although it was not statistically significant in our study, PFS rates were shown to be lower in relapsed patients than in others.

In fact, grade I meningiomas are more frequently included in SRS/SRT studies due to their high incidence. These lesions have been image-diagnosed, it is difficult to distinguish them from malignant meningiomas except for some special imaging techniques, but these imaging techniques are not included in routine applications.[13] On the other hand, we encounter series that include patients with a history of surgery who underwent radiosurgery due to recurrence or residue. Such studies allow a more accurate assessment of the relationship between meningioma grade and survival outcomes. Low grade patients were included in some of the studies in which SRS/SRT was applied due to postoperative residue or recurrence, but we also come across a limited number of studies in which grade 2 or even grade 3 patients were added.[9] In this context, it was emphasized that PFS worsened with increasing grade in a retrospective series.[7] Grade 2 meningiomas constituted a quarter of the patients included in our study. Similarly, PFS was shown to be adversely affected in grade 2 cases. In another study, SRS was applied to 75 grade 2 meningioma cases due to postoperative residual or recurrence.[14] The 5-y OS was determined as 81.1% and the 5-y PFS as 55.7%. In our study, the 5-y PFS was found to be similar to this study with a rate of 57.7%, but no difference was found in terms of OS according to grade.

Another important parameter affecting the treatment response is the size or volume of the tumor, which has been emphasized in many studies.[6,15] Manabe et al.[15] reported that tumor size <3 cm (<13.5 ml) had a better PFS, and tumor control was difficult in patients with a tumor size greater than 3 cm. Dibiase et al.[6] reported that both OS and PFS were significantly worse in patients with tumor volume above 10 cc. In our study, a positive correlation was shown between tumor diameter less than 2 cm and PFS. Furthermore, in a very large retrospective study involving 4565 patients, it was reported that PFS decreased if the number of lesions was greater than 1.[8] We also found that the number of lesions affected both OS and PFS in our study, and we found that it remained prognostic for PFS in the multivariate analysis.

While applying SRS/SRT, the questions of whether it is a single fraction or multiple fractions and which patient, have been one of the main subjects of the studies as well as in our daily practice. In the meta-analysis published in 2022, which included 20 studies and over 1400 patients, it was observed that 5-y results did not change when single fraction and multiple fractions schemes were compared.[16] In our study, no difference was observed in terms of OS and PFS with single or multi-fractionated RT. In our study, the main reason for the preference of multi-fraction treatments was the presence of larger tumors and tumors close to critical structures, as in other studies.

Unfortunately, there are limitations of our study. Despite the 5- and 7-year results, the study was highly heterogeneous. One reason for this was the inclusion of patients with image-diagnosed meningioma who underwent radiosurgery, as well as patients who underwent radiosurgery for post-operative residual or recurrent disease. Another reason is that both grade 1 and grade 2 patients were included and the grade of meningioma was not included in the study inclusion criteria. Also, its retrospective design may lead to the possibility of selection bias. Due to its retrospective nature, symptomatic response and treatment-related toxicity assessment could not be defined in detail, although complaints were recorded during the follow-up period.

CONCLUSION

Since SRS/SRT can provide high tumor control in the management of meningioma, it can be preferred as an alternative treatment method, especially in patients who are diagnosed radiologically, who are not candidates for surgery or who refuse surgical treatment, as well as in cases of residual and recurrence in the post-surgical period.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by The University of Health Sciences, Samsun Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (No:2021/12/3, Date:23.6.2021)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Kohler BA, Ward E, McCarthy BJ, et al. Annual report to the nation on the status of cancer, 1975-2007, featuring tumors of the brain and other nervous system. J Natl Cancer Inst 2011;103(9):714-36.
2. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. J Neurol Neurosurg Psychiatry 1957;20(1):22-39.
3. Goldbrunner R, Stavrinou P, Jenkinson MD, et al. EANO guideline on the diagnosis and management of meningiomas. Neuro Oncol. 2021;23(11):1821-34.
4. Valentino V. Radiosurgery in cerebral tumours and AVM. Acta Neurochir Suppl (Wien) 1988;42:193-7.
5. Bir SC, Patra DP, Maiti TK, Bollam P, Minagar A, Nanda A. Direct Comparison of Gamma Knife Radiosurgery and Microsurgery for Small Size Meningiomas. World Neurosurg 2017;101:170-9.
6. DiBiase SJ, Kwok Y, Yovino Si et al. Factors predicting local tumor control after gamma knife stereotactic radiosurgery for benign intracranial meningiomas. Int J Radiat Oncol Biol Phys 2004;60(5):1515-9.
7. Kondziolka D, Mathieu D, Lunsford LDi et al. Radiosurgery as definitive management of intracranial meningiomas. Neurosurgery 2008;62(1):53-8; discussion 58-60.
8. Santacroce A, Walier M, Régis J et al. Long-term tumor control of benign intracranial meningiomas after radiosurgery in a series of 4565 patients. Neurosurgery 2012;70(1):32-9; discussion 39.
9. Cohen-Inbar O, Lee CC, Sheehan JP. The Contemporary Role of Stereotactic Radiosurgery in the Treatment of Meningiomas. Neurosurg Clin N Am 2016;27(2):215-28.

10. Leroy HA, Tuleasca C, Reyns N, Levivier M. Radiosurgery and fractionated radiotherapy for cavernous sinus meningioma: a systematic review and meta-analysis. Acta Neurochir (Wien) 2018;160(12):2367-78.
11. Ruge MI, Tutunji J, Rueß D, et al. Stereotactic radiosurgery for treating meningiomas eligible for complete resection. Radiat Oncol 2021;16(1):22.
12. Pou P, Biau J, Verrelle P, et al. Long-Term Outcomes After Linac Radiosurgery for Benign Meningiomas. Clin Oncol (R Coll Radiol) 2020;32(7):452-8.
13. NCCN.org [homepage on the Internet]. Pennysylvania: National Comprehensive Cancer Network [updated 2.2002; cited 24 February 2023]. NCCN Guidelines Version 2.2022 Meningiomas, Available from: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf
14. Refaat T, Gentile M, Sachdev S, et al. Gamma Knife Stereotactic Radiosurgery for Grade 2 Meningiomas. J Neurol Surg B Skull Base 2017;78(4):288-94.
15. Manabe Y, Murai T, Ogino H, et al. CyberKnife Stereotactic Radiosurgery and Hypofractionated Stereotactic Radiotherapy As First-line Treatments for Imaging-diagnosed Intracranial Meningiomas. Neurol Med Chir (Tokyo) 2017;57(12):627-33.
16. Bin-Alamer O, Alnefaie N, Qedair J, et al. Single session versus multisession stereotactic radiosurgery for the management of intracranial meningiomas: a systematic review and meta-analysis. J Neurooncol 2022 Aug 17. doi: 10.1007/s11060-022-04112-6.