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Gamma knife radiosurgery for central arteriovenous malformations: a single-center experience

Santral yerleşimli arteriyovenöz malformasyonlar için gamma knife radyocerrahisi-tek merkez deneyimi

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Abstract

Purpose: Arteriovenous malformations with basal ganglia, brainstem, and thalamic locations represent complex vessel anomalies with critical areas. Treatment of these central lesions is related to high morbidity and mortality rates. This retrospective study aims to examine the results of our clinic's patients with basal ganglia, brainstem, and thalamic arteriovenous malformations remedied with gamma knife radiosurgery (GKS).

Material and method: The results of patients with basal ganglia, thalamus, and brainstem located AVM who underwent GKS from May 2005-December 2020 were analyzed in the Gazi University Gamma Knife Unit.

Results: A total of 859 patients with intracranial AVM were treated at the Gamma Knife Unit of the Gazi University Neurosurgery Clinic between May 2005-December 2020. Seventy-three patients with basal ganglia, brainstem, and thalamic locations were recorded. In a total of 73 patients who were included in the study, the lesion was located in the basal ganglia in 14 (19.2%), the brainstem in 13 (17.8%), and the thalamic region in 46 (63%) patients. The mean volume of AVMs was 4565.54 mm^3. The patients who underwent embolization before gamma knife surgery treatment were found to be 19.2%. The mean of AVMs' obliteration time after SRS is 38.4 months. We detected that there was no significant statistical rate relationship between obliteration rate and AVMs volume, Spetzler - Martin Grading Scale, nidus type, gender, and prior embolization (p>0.05).

Conclusions: GKS is one of the effective choice treatment methods used for cerebral AVMs today. Furthermore, it has been accepted as the first choice treatment method, especially in central AVMs, which are risky in terms of mortality and morbidity, and also with good outcomes.

Key words: Arteriovenous malformations, stereotactic radiosurgery, gamma knife radiosurgery, basal ganglia, thalamus.

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Öz

Amaç: Bazal gangliyon, beyin sapı ve talamik yerleşimli arteriovenöz malformasyonlar (AVM) kritik bölgede yerleşmiş kompleks damar anomalileridir. Bu santral yerleşimli lezyonların tedavisi yüksek morbidite ve mortalite riski taşır. Çalışmamızda bazal ganglion, beyin sapı ve talamik yerleşimli AVM nedeniyle kliniğimizde gamma knife radyocerrahi uygulanmış hastaların sonuçları retrospektif olarak incelenmesi amaçlandı.

Gereç ve yöntem: Mayıs 2005-Aralık 2020 tarihleri arasında Gazi Üniversitesi Gamma Knife Ünitesinde tedavi edilmiş bazal gangliyon, talamus ve beyin sapı yerleşimli AVM hastalarının sonuçları incelendi.

Bulgular: Mayıs 2005-Aralık 2020 tarihleri arasında Gazi Üniversitesi Gamma Knife Ünitesinde toplam 859 intrakraniyal AVM hastası tedavi edildi. Bazal ganglion, beyin sapı ve talamik lokalizasyonu olan 73 hasta çalışmaya dahil edildi. Çalışmamıza dahil edilen toplam 73 hastanın 14'ü (%19,2) bazal ganglionda, 13'ü (%17,8) beyin sapında ve 46'sı (%63) talamik bölgede yer alıyordu. Ortalama AVM hacmi 4565,54 mm^3 olarak hesaplandı. Gamma knife cerrahisi tedavisinden önce embolizasyon uygulanan hastaların oranının %19,2'idi. SRS sonrası AVM'lerin ortalama tam kapanma sürelerinin 38,4 aydı. AVM hacmi, Spetzler Martin derecelendirme ölçeği, nidus tipi, cinsiyet ve önceki embolizasyon ile kapanma oranı arasında istatistiksel olarak anlamlı ilişkisi saptanmadı (p>0,05).

Sonuç: GKS günümüzde serebral AVM tedavisinde kullanılan etkin bir tedavi yöntemidir. GKS özellikle tedavisi yüksek morbidite ve mortalite riski içeren santral yerleşimli AVM tedavisinde başarılı sonuçları ile öncelikli tercih edilen tedavi yöntemlerindendir.

Anahtar kelimeler: Arteriyovenöz malformasyonlar, stereotaktik radyocerrahi, gamma knife radyocerrahisi, bazal ganglionlar, talamus.

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Introduction

The central location's arteriovenous malformations (AVMs) constitute 3-13% of all intracranial AVMs [1]. Due to the critical area of these AVMs, they must be treated with early intervention [2]. Due to the deep location of the basal ganglia, brainstem, and thalamic AVMs, as well as the narrow study corridors, surgical resections are related to relatively poor obliteration rates and higher persistent neurological morbidity rates [3]. For this reason, stereotactic radiosurgery (SRS) has become the preferred treatment method in this patient group [4]. This study aims to review our experiences with gamma knife radiosurgery (GKS) in treating of basal ganglia, thalamus, and brainstem arteriovenous malformations and to evaluate the results in these patients.

Materials and methods

Patient population

A total of 859 patients with intracranial AVM were treated at the Gamma Knife unit of the Gazi University Neurosurgery Clinic between May 2005-December 2020. The primary patient data included AVM and SRS treatment variables. In addition, patient variables consisted of age, gender, previous AVM bleeding criteria, prior embolization, AVM volume, and The Spetzler - Martin score and Gamma Knife data of each patient were calculated.

The patients were analyzed retrospectively, and 73 patients with basal ganglia, thalamus, and brainstem locations were seen. Patients were included with a follow-up of at least two years in the study.

Radiosurgical procedure

Our SRS technique for AVMs was performed under local or monitored anesthesia, and the patient's calvarium was enclosed in a Leksell frame. SRS was performed using digital cerebral angiography (DSA) and Gamma Knife unit based on angiography of AVM nidus defined by contrast thin slice (1-2 mm) Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) when MRI was contraindicated.

Follow-up

Follow-up with radiological imaging was recommended at intervals of 6 months for clinical evaluation of the patients. Angiography was used to prove the obliteration of the AVM nidus. Control angiograms were planned to be two years after GKS treatment.

Statistical analysis

All factor categories were analyzed using the chi-square and T-test. Statistical analysis was performed using the SPSS 2020 software. A *P*-value of ≤0.05 was considered significant.

Permission was obtained from Gazi University Clinical Research Ethics Committee for the study.

Results

In a total of 73 patients included in our study, the lesion was located in the basal ganglia in 14 (19.2%), the brainstem in 13 (17.8%), and the thalamic region in 46 (63%) patients. The mean age of the patients was 25.14 years. Thirty-seven patients (50.7%) were male, and thirty-six patients (49.3%) were female. There was no noticeable gender difference in terms of AVMs locations (Table 1).

The mean SRS margin doses were 20.2, and the maximum was 39 Gy. The mean number of isocenters was 8.95. The mean volume of AVMs in the basal ganglia was 3885 mm^3, the mean volume of brainstem AVMs was 12300 mm^3, and the volume of thalamic AVMs was 14800 mm^3 (Table 2). According to the Spetzler - Martin grading scale, grade 1 AVMs and grade 5 AVMs ratios were equal to 2.7% (2/73) (Figure 1). Diffuse nidus AVMs were observed more

Table 1. Anatomical locations of 73 patients with central AVMs

Location	Patient (n) – Valid Percent (%)
Basal Ganglion	14-19.2
Brainstem	13-17.8
Thalamic	46-63.0
TOTAL	73-100

frequently in brainstem-located AVMs (23.1% (3/13)), while compact nidus was observed more frequently in basal ganglia-located AVMs (92.9% (13/14)). The patients who underwent embolization before SRS were found to be 19.2%. And, the basal ganglia, brainstem, and thalamus AVMs were found to be 23.6% (4/14), 23.1% (3/13), and 15.2%, respectively (7/46) (Table 3).

In general, the total rate of minor and major complications was 21.9% (16/73), while the highest rate of complications according to the location was found to be in the brain stem at a rate of 28.5% (4/14) (Figure 2).

The most common clinical presentation was a headache at 37% (27/73) in all locations, followed by bleeding at 17.8% (13/46). In follow-up, bleeding was seen at 7.1% in basal ganglia AVMs and 2.2% in thalamic AVMs after gamma knife surgery, while no bleeding was observed in the brainstem during follow-up.

The mean of AVMs' obliteration time after SRS is 38.4 months. There was no significant difference between the obliteration after SRS to the location. Obliteration rates were detected at 64.3% (9/14) in basal ganglia AVMs, 61.5% (8/13) in brainstem AVMs, and 60.9% (18/46) in thalamic AVMs. AVMs were followed without complications and did not obliterate during

Table 2. Age (year), Follow-up (month), Prescription dose, and AVM Volumes (mm^3) tables of patients with central AVMs according to locations

Location		Minimum	Maximum	Mean
BASAL GANGLION	Age	12	36	23.36
	Follow-up	24	71	37.21
	Prescription dose	14	25	21.00
	AVM Volume	16	11170	3885.00
BRAIN STEM	Age	8	50	32.54
	Follow-up	24	77	48.08
	Prescription dose	14	22	17.00
	AVM Volume	184	12300	2680.08
THALAMIC	Age	7	66	23.59
	Follow-up	23	112	37.72
	Prescription dose	16	24	19.52
	AVM Volume	538	14800	5321.96

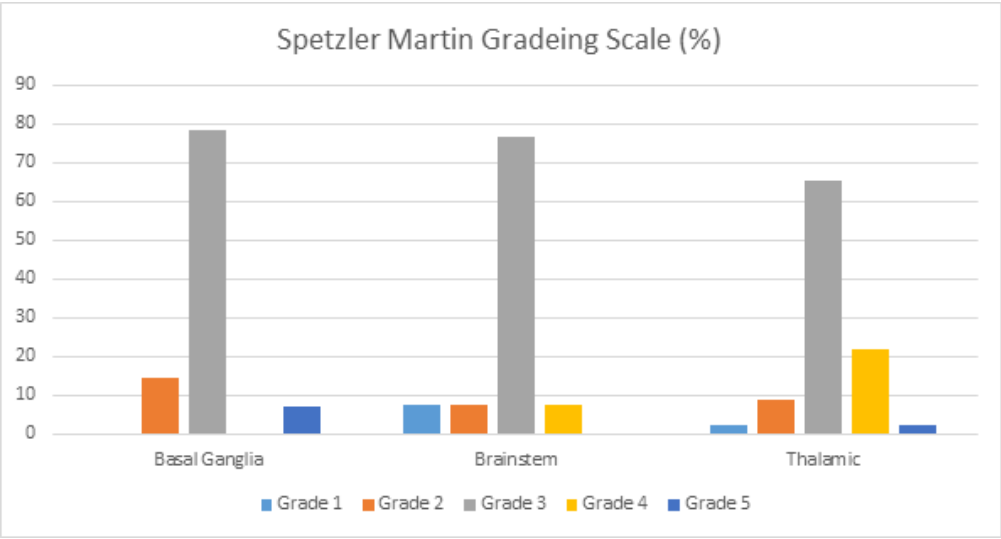

Figure 1. Distribution of central AVMs according to the Spetzler Martin Grading Scale

Table 3. Prior embolization rates of Central AVMs

Location	Embolizatıon	Patient (n) –Valid percent (%)
BASAL GANGLION	+	9-64.3
	-	5-35.7
	Total	**14-100.0**
BRAIN STEM	+	8-61.5
	-	5-38.5
	Total	**13-100.0**
THALAMIC	+	28-60.9
	-	18-39.1
	Total	**46-100.0**

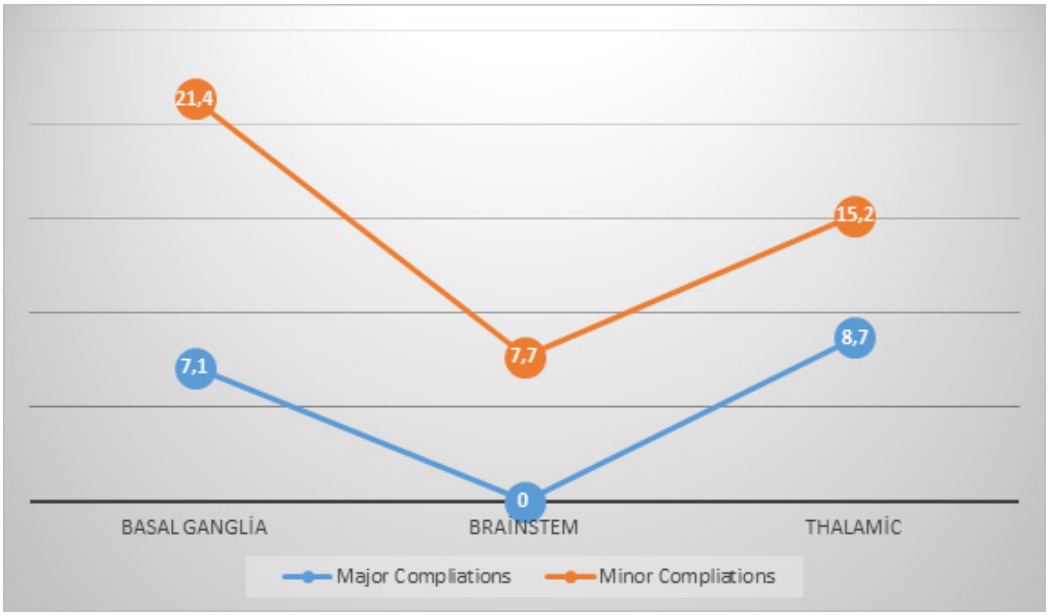

Figure 2. The prevalence value percents of major and minor complications after SRS

follow-up and were seen at 2.7% (2/73). Additionally, our study detected that there was no significant statistical rate relationship between obliteration rate and AVMs volume, Spetzler - Martin grading scale, nidus type, gender, and prior embolization (p>0.05).

Discussion

Cerebral arteriovenous malformations of the central locations denote vascular anomalies that are difficult to manage and carry significant lifelong risks for patients. In addition, they created a very high-risk subgroup with intracranial AVMs due to the very high annual bleeding risks related to increased mortality and morbidity rates.

Central AVMs constitute about 3-13% of all intracranial AVMs [5]. Nicolato et al. [6] stated that the bleeding rate was 51% in patients with cortical AVMs and said that it increased up to 91% in patients with central AVMs. Even more, Sasaki et al. [7] found that the annual risk of bleeding was higher in patients with central AVMs. A large proportion of patients with central AVMs, such as 86-91%, presented with bleeding [7]. This high incidence of bleeding in central AVMs can be explained by the high perfusion pressure-venous pressure and the higher incidence of related vascular aneurysms in this location [8].

Surgical excision is the complete resection of AVMs by craniotomy, a definitive treatment method [9]. However, both associated with

a greater risk of bleeding associated with conservative treatment the higher the risk of complications as a result of both resection, SRS for brainstem, basal ganglia, and thalamic AVMs has emerged as a therapeutic option, and after one session of 40-86% obliteration rates was provided [2, 10]. Gross et al. [3] detected resection results for the thalamus and basal ganglia AVMs. Overall, they recorded a complete resection rate of 91% and a mortality rate of 2.4% (the deficit rate between 13% and 33% among the reports) [3, 11].

Embolization can be used only with resection or SRS to treat AVMs because embolization can destroy many AVMs and also relate to significant morbidity [12, 13]. For example, persistent morbidity rates after embolization in basal ganglia, brainstem, and thalamic AVMs vary from 11% to 40% [13, 14].

Central AVM obliteration rates of 4 or 5 years were 66% and 86%, and permanent morbidity rates changed between 4% and 17% [13-15]. Pollock et al. [16] reported 10 cases in the basal ganglia, 30 in the thalamus, and 16 in the brainstem. Complete obliteration was reported in 24 (43%) of 56 patients after SRS at an average of 45 months. Koga et al. [15] reported total obliteration rate of thalamic AVMs for five years after SRS treatment was 82%. Sasaki et al. [7] found high morbidity and mortality rates in basal ganglia and thalamic AVMs patients who underwent conservative or only embolization compared to radiosurgery.

The first goal of the SRS is the destruction of the nidus [17]. Many studies have suggested that a higher margin dose increases the obliteration rate [9, 15, 18]. In the current series, it has been noted that in patients who had previous bleeding and had a smaller nidus volume, total obliteration occurred with a high margin dose [18]. But along with this, Choi et al. [19] found that the 20 higher marginal doses (≥20 Gy) were not related to obliteration, as in our study. In addition, it has been said that hormonal differences might contribute to the different hypersensitivity of AVMs to SRS in male and female patients, unlike our study. Some studies have recorded the relationship between progesterone and vascular endothelial growth factor [2, 6]. However, our series observed no practical difference between the genders of AVMs obliteration. Different from our results, fewer obliteration rates after SRS has been reported in bigger AVMs and Spetzler - Martin grade ≥4 AVMs [20]. Again, it has been reported that the incidence of SRS complications is higher in larger AVMs [21]. In brief, although there is no significant relationship between our series data, it has been reported that the dose, the number of isocenters, the previous bleeding, and the compactness of the nidus can be considered a prognostic factor of clinical outcomes for AVMs after SRS.

In conclusion, obliteration rates are poor in the central AVMs. In contrast, the incidence of mortality and morbidity is higher. We believe that SRS has a critical role in AVMs of basal ganglia, thalamic, and brainstem lesions, which are considered to involve extreme risk for surgical removal. The best choice for SRS are patients with a central location and a smaller volume AVM suitable for receiving at least 20 Gy at the margin.

Conflict of interest: No conflict of interest was declared by the authors.

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Ethics committee approval: Permission was obtained from Gazi University Clinical Research Ethics Committee for the study (date: 19.10.2020 and number: 2022-977).