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The Efficacy of Gamma Knife Radiosurgery for Arteriovenous Malformations: One-Year Monitor for 105 Iraqi Patients.

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ABSTRACT
Objective: Cerebral arteriovenous malformations (AVM) are inborn errors and benign lesions, majorly found in the young and healthy population. This study aimed to evaluate the efficiency of Gamma Knife radiosurgery (GKRS) in the management of AVMs and to predict any complications during the 12 months post therapy.
Material and Methods: We reviewed 105 patients who were treated with GKRS for intracranial AVMs between January 2016 and March 2018. Participants included 48 male and 57 female patients with a mean age of 27 years. AVM volumes were assessed using MRI at every 3 months.
Results: The results of this study revealed a significant shrinkage in the volume of the AVMs, in particular, for those with less than 3 cm^3 with P < 0.0001.
Conclusion: GKRS is considerably efficient in the treatment of AVMs.
Keywords: Arteriovenous malformations, Radiosurgery, Gamma Knife
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INTRODUCTION

Radiosurgery is well-known therapy, designated particularly for treating tumors, vascular abnormalities, and functional illnesses [1]. Extensive medical intervention is necessary in this procedure, considering the type of the lesion, pathology if accessible, locations in addition to the age, and overall health of the patient [2]. Gamma Knife, the recent radiosurgery, uses radiation targeted precisely to the abnormal target site in order to avoid destruction of healthy brain tissue [3]. Gamma Knife radiosurgery (GKRS) is able to precisely focus the gamma rays on one or more target. Each single ray is of relatively low intensity to ensure diminutive influence on the intervening tissue of the brain [4]. GKRS is proven to be effective for patients with vascular malformations such as an arteriovenous malformation (AVM), several tumor types, and functional issues [5]. Although the patients can be treated within 1–5 days as outpatients (in contrast to the 15 days of ordinary hospitalization for a craniotomy), the results of GKRS may not be clearly seen until several months after the treatment [6].

PATIENTS AND METHOD

We reviewed and had a follow-up of 105 patients between January 2016 and March 2018 (48 males with mean age 27.1 ± 10.93 and 57 females with mean age 27.05 ± 10.83) who were treated with GKRS for intracranial AVMs in the Neuroscience Hospital in Baghdad, Iraq. GKRS was applied for patients who are candidate for such therapy. The patients were categorized into four groups according to the size of their AVMs using Spetzler–Martin grading system, which was established for the surgical resection, and their suitability for RS was considered [7]. The features of these patients are summarized in Table 1.

Table1: The presenting feature of the patients

Group	Seizure (%)	Bleeding (%)	Patient count (n)
1 (<3 cm^3)	10	90	29
2 (3–6 cm^3)	92	8	9
3 (>10 cm^3)	91	9	47
4 (abnormal figure)	59	41	20

Gamma Knife Radiosurgery Procedure

All patients underwent stereotactic radiosurgery with Leksell Gamma Knife Unit model perfexion—Co60 source (A.B. Elekta, Stockholm, Sweden, 2014). The technique was commenced by setting the Leksell stereotactic coordinate frame using local anesthesia. Preoperative magnetic resonance imaging (MRI) with contrast and 1 mm slice thickness was achieved for all patients. Attained images were subjected to Gamma-Plan treatment planning system. Target dimensions were demarcated by the neurosurgeon on the MRI images. Treatment was planned with 4, 8, and 16 mm collimators using single or multiple shots to ensure target coverage. Plans were then executed using the treatment machine through network system and the patients were treated with automatic or manual positioning systems.

Three caps were used on our frame:
First: to adapt the frame to the gutter of the collimator.
Second: to measure the skull frame dimensions.
Third: to fill the indicator with $CuSO_4$ for MRI study.
The radiation doses are summarized in Table 2.

Table 2: The radiation doses

Size of AVMS	Dose/gray
<3 cm^3	20
3–6 cm^3	22

>6 cm^3	24
Abnormal figures	25

The overall procedure takes 15–30 min. The final step includes removing the screws from the patients head and discharging them on local analgesia on the same day.

Follow-up Rules

Follow-up procedure involved clinical examination and MRI at 3, 6, 9, and 12 months posttherapy. The AVMS volumes were measured manually to confirm the far-off response.

Statistical Analysis

All statistical tests were achieved by using Microsoft Excel statistical package, which operates under Windows operating system. Data were expressed as mean + standard deviation. Differences between the mean values were analyzed using paired t-test. A P value <0.05 was considered as statistically significant.

RESULTS

In total, 105 patients with several AVM sizes were subjected to GKRS; their characteristics are presented in Table 3.

Table 3: The characteristics of the studied group

	Male	Female
Total patient count (n)	48	57
Age	27.1 ± 10.93	27.05 ± 10.83
Small AVM (<3 cm^3)	12	17
Medium AVM (3–6 cm^3)	5	4
Large AVM (>6 cm^3)	22	25
Abnormal figure AVM	9	11

MRI follow-up analysis up to 1 year post radiosurgery revealed the following results.

1- Group 1 with small size AVMs: The AVMs overall reduced by 47% of their original volume (mean value reduced from 1.299 ± 0.597 to 0.696 ± 0.293, P < 0.0001) at 12 months post therapy (Fig. 1). Unfortunately, the data for 3, 6, and 9 months were insufficient due to lack of patient follow-up.

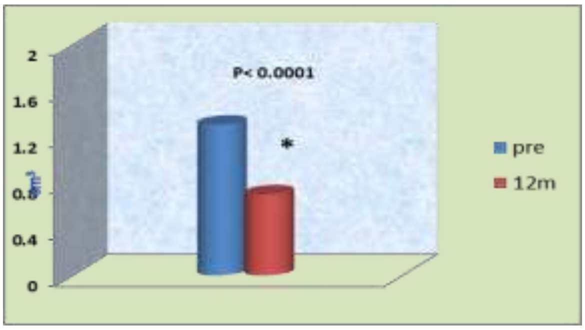

Fig.1: Small size AVM (no. =29)

2- Group 2 with medium size AVMs: A significant shrinkage of AVMs volumes was observed by 10% (P < 0.005) and 43% (P < 0.0001) after 3 and 12 months, respectively.

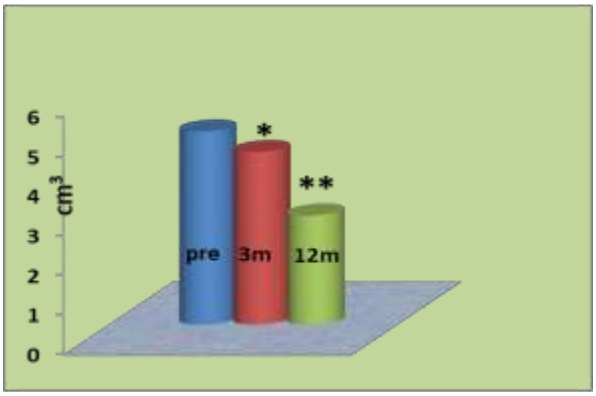

Fig. 2: Medium size AVM (no. =9), * P< 0.005, **P< 0.0001

3- Group 3 with large size AVMs: As in previous groups, a significant reduction in the AVM volumes by 11% and 43% (P < 0.0001) were found after 3 and 12 months, respectively (Fig. 3).

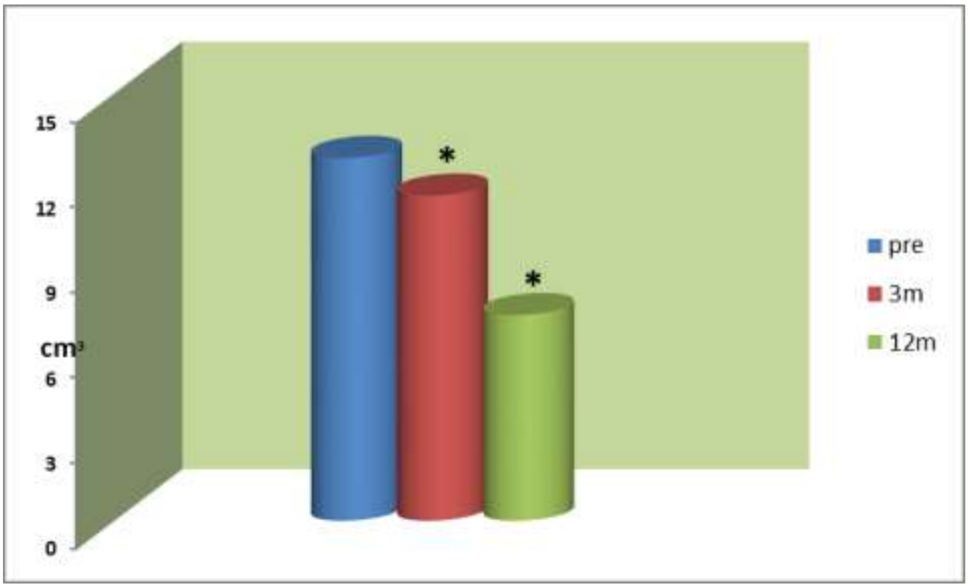

Fig.3: Large size AVM (n = 47) *P < 0.0001

4- Group 4 with abnormal figure: The AVM volumes were obtained by multiplying the longest three dimensions divided by two [7]. Although the reductions were 12%, 18%, and 28% of its original size at 3, 6, and 12 months, respectively, which is less than the other groups, they were statistically substantially significant with P < 0.001 (Fig. 4).

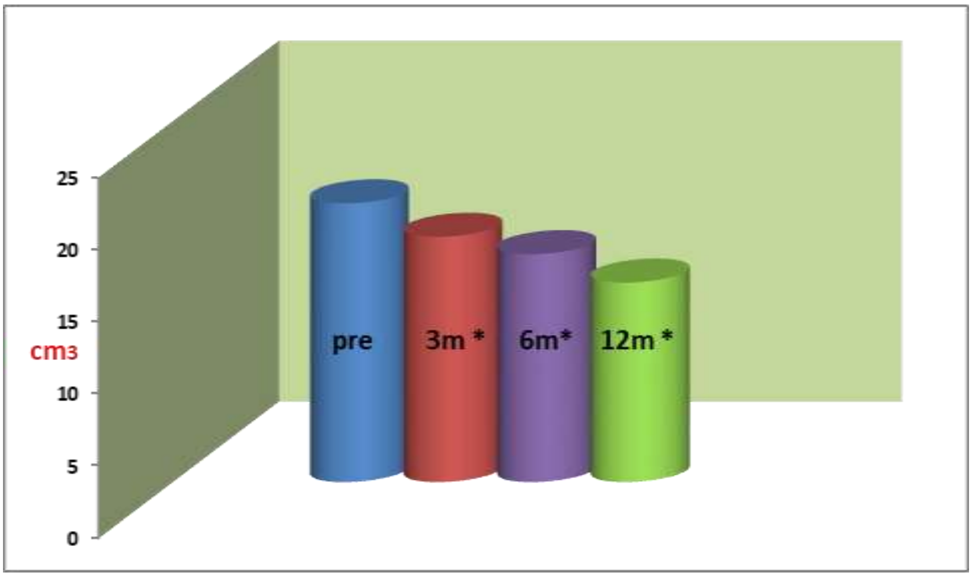

Fig. 4: Abnormal figure AVM (no. = 20), *P< 0.0001

DISCUSSION

Epidemiologically, about 0.1% of the populations reveal AVM [8, 9]. Each gender is correspondingly affected. AVMs are the foremost reason of non-traumatic intra-cerebral hemorrhage in people aged less than 35 years [10]. Several treatments were considered depending on a number of elements, for instance, the site, dimension, history of hemorrhage in addition to the patient age, and the general medical circumstances including surgery, catheter embolization, and radiosurgery [11]. In this study we evaluated the response of AVMs to radiotherapy, since such therapy induces vascular damage that proceeds to gradual sclerosis of blood vessels [12]; we took a follow-up of the volume changes throughout 12 months (every other 3 months). These volume changes reflect the rate of obliteration of AVMs [13]. For appropriate assessments, we categorized the AVMs according to their size into four groups. Interestingly, all groups revealed dramatic shrinkage in their volumes by approximately 10% (P < 0.005) of their original volume, which started as early as 3 month post therapy. Moreover, the patients with small size AVMs (less than 3 cm3) revealed the highest decrement in their volume which reached 47% (P < 0.0001) of its original size, 1 year post GKRS. Notably, these findings are in accordance with the previous studies (14, 15, 16) however, AVMs with abnormal figures reveal least response at the end of first year, which is only 28% of their original size; this could be due to poor targeting of the radiation beam and scattering effect. Furthermore, in the present study, we noticed that the intracranial bleeding is the most common presentation of small AVMs, whereas the larger ones tend to induce seizure attacks; these findings are established by Hernesniemi et al. and approved by the American Heart Association [17,18]. Unfortunately, the limitation of our study is the lack of patients during the follow-up schedule; we should extend the follow-up periods up to 5 years, the time by which the obliteration rate reached 78%, which is especially implicated for larger AVMS [19].

CONCLUSION

GKRS is an effective, prosperous, and harmless procedure for AVMs with remarkable response, in particular, for those less than 3 cm3.

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