ORIGINAL PAPER

The Visualization and Frequency of Cerebral Cavernous Angioma on Magnetic Resonance

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ABSTRACT

Background: Cavernous angiomas (CAs) are abnormal, congenital, vascular malformations, which often grow in size over the course of life. Conservative treatment, microsurgical resection, and stereotactic radiosurgery are the three main options for treatment of CA. Radiological studies play a key role in diagnosis, with magnetic resonance (MR) being the method of choice. **Objective:** The aim of this study was to establish the prevalence of cavernous angiomas, the size, appearance, that is, the type of CAs and to determine visualization of cavernous angiomas by magnetic resonance. **Methods:** The study included all patients who underwent an MR of the brain in the period from January 2011 to the end of December 2017 at the Radiology Clinic of Tuzla University Clinical Centre, and in whom MR examination verified one or more CAs. **Results:** The prevalence of cavernous angioma in the study was 0.57%, and men and women were equally represented. The number of cavernous angiomas per patient was between 1 and 79 ; the average diameter was 11mm, and the most common type at ≥ 3mm was equivalent to Type II, whilst the largest number of cavernous angiomas, regardless of the size and visualization on individual sequences, were equivalent to Type IV. No significant difference was found in sensitivity between spin echo sequence and T2W gradient echo sequence in the group comprised of cavernous angiomas ≥ 3mm, whilst in the group comprised of punctiform cavernomas < 3mm, T2W* was a significantly more sensitive sequence than spin echo, that is, spin echo sequence had significantly lower sensitivity in the detection of punctiform CAs. **Conclusion:** The prevalence of CAs was in line with the results of other studies. T2W* sequence is significantly more sensitive in comparison with spin echo only in the detection of punctiform CAs, and is important in the detection of multiple familiar CAs.

Keywords: cavernous angioma, venous angioma, association, visualization, magnetic resonance.

1. BACKGROUND

Cavernous angiomas (CAs), also known as cavernous malformations, cavernous hemangiomas or cavernomas, are congenital, abnormal vascular malformations, which frequently increase in size over the course of life. The expressions "hemangioma" and "cavernous" are incorrect because these are neoplastic lesions (1). CAs are the second most common vascular malformation of the brain, and they typically present in the formation of multiple lumens and vascular leakage on the level of the capillaries of the brain, which results in disruption of the blood-brain barrier (2). Patients with intracranial CAs may be asymptomatic, or symptomatic with headaches, epileptic attacks, or intracerebral bleeding (3). Symptoms caused by CAs may occur in only 40% of patients over the course of life (1). The exact prevalence of CAs is unknown because many patients with CAs are asymptomatic. Autopsy studies estimate that the prevalence of CAs is between 0.2% and 0.5% (4). These lesions have slow blood flow and low pressure, meaning that the risk of rupture is lower than in some other vascular malformations, such as arteriovenous (AV) malformations. Cortico-subcortical CAs have a lower risk of intracerebral hemorrhage, in contrast

to those more deeply located (5). The clinical symptoms of CAs usually appear between 20 and 50 years of age (at an average age of about 30 years), but they may also occur in early childhood or old age (6). Conservative treatment, with control of symptoms and monitoring, microsurgical resection, and stereotactic radiosurgery are the three main options for treatment of CAs. (7). In some cases, targeted radiotherapy is used for treating lesions which are inaccessible by surgery (5, 7). The total mortality related to bleeding from CAs is low, estimated at 2.2%, but progressive neurological deficits may accumulate and reduce the patient's quality of life (8). Radiological studies play a key role in the diagnosis of cerebral CAs, with magnetic resonance (MR) being the method of choice. (1).

2. OBJECTIVE

The aim of this study was to establish the prevalence of cavernous angiomas, the size and appearance, that is, the type of CA, and to determine the visualization of cavernous angiomas by magnetic resonance.

3. MATERIAL AND METHODS

This research had the character of a retrospective study, conducted at the Clinic for Radiology and Nuclear Medicine of the Institute of Public Health at Tuzla University Clinical Centre. The study included all patients who underwent an MR of the brain in the period from January 2011 to the end of December 2017, and in whom MR examination verified one or more CAs. Their MR images were stored in the PACS *(Picture Archiving and Communication System)* system of the Clinic, whilst the written results, interpreted by one of three radiologists, are kept in the Radiology Information System–RIS. After examination of the RIS records of 11,502 patients who underwent MR of the brain, all the patients were selected for whom the conclusion of the results confirmed a pathological substrate known as cavernous angioma, cavernoma or cavernous malformation (in view of the differing terminology and synonyms used for CAs). The number of subjects in the study was 66. All those patients were excluded from the study who did not undergo a post-contrast MR examination, along with patients with extensive acute haemorrhage in the CA which could "conceal" an existing VA, that is, give a false negative finding, and patients in whom the T2W gradient echo showed a round shaped absence of signal, for which it could not be said with certainty whether it was indicative of a CA or chronic microhemorrhages. Native and contrast MR recordings of the brain were performed on one of two 1.5 Tesla MR machines, a Siemens machine (Avanto model, Erlangen, Germany) or a Philips machine (Netherlands). According to the number of CAs diagnosed in each patient, we divided the subjects into 5 groups: patients with one CA, patients with two CAs, patients with three CAs, patients with four CAs, and patients with multiple CAs (five or more CAs). According to the size of the Cas, they were deemed to be punctiform if they were <3mm on the spin echo or gradient echo sequences; or larger non-punctiform if on the spin echo sequences they were ≥3mm, and giant if the diameter of the CA was greater than 6 cm. The following were analysed: the number of individual CAs per patient, the size, appearance (that is type) of CA, and visualization of the CA on T1W and T2W spin echo sequences.

Statistical analysis of data

The data collected were stored in a database created in the commercial program Microsoft Access. In the standard analysis, standard descriptive statistical methods were used (mean values and standard deviation) and standard statistical parameters. The comparison of the sizes of the CAs between genders was tested using the T-test. The differences in frequency of Cas between men and women, and the differences in sensitivity of native and contrast MR studies in visualization of CAs were tested using the chi-square test. The statistical hypotheses were tested on a level of significance of a=0^5; that is, differences on the level of p<0.05 were deemed significant.

4. RESULTS

In this retrospective study, that ran from January 2011 to the end of December 2017, the presence of one or more CAs was confirmed in 66 patients (0.57%) out of the 11,502 patients who underwent MR of the brain. Of these 66 patients, who were aged 1 to 78 years, 33 (50%) were male, whilst the remaining 33 (50%) were female. There was no significant difference between the number of male and female subjects (p=0.88; χ^2=0.22). The average age of all the subjects was 47.68 ± 18. 96 (the lowest age was 1 year and the highest 79 years). The average age of the men was 48 ± 15.13; and of the women 47.3 ± 22.38 years. Fig. 1 shows the distribution of subjects in age groups. The highest number of subjects, 24.3%, were in the 60 to 70 years age group, and the smallest number, 6.1%, were in the 20 to 30 years age group. There were three children aged 1-14 (4.5%) in the study.

A total of 176 CAs were verified in the 66 subjects. Of these, 86 CAs had a diameter of ≥3mm and there was a further 90 CAs that were only visible on T2W gradient echo sequence

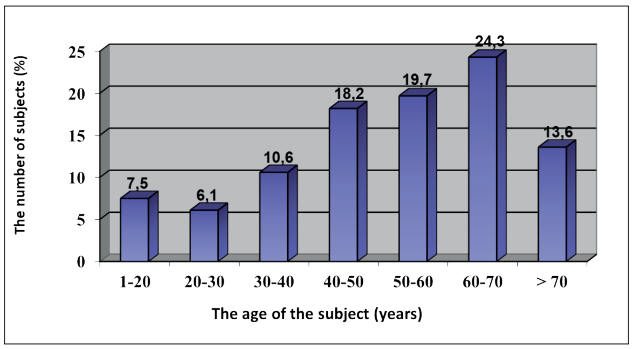

Figure 1. The distribution of subjects according to age groups

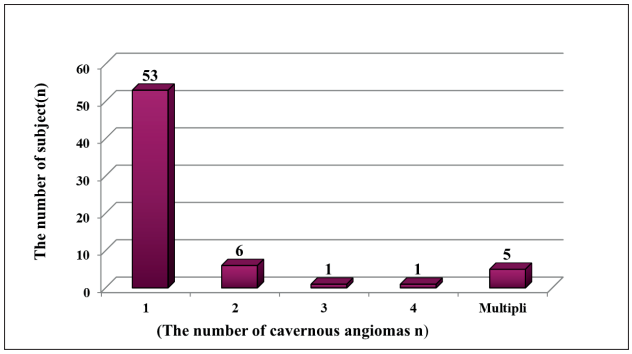

Figure 2. The distribution of subjects according to the number of cavernous angiomas

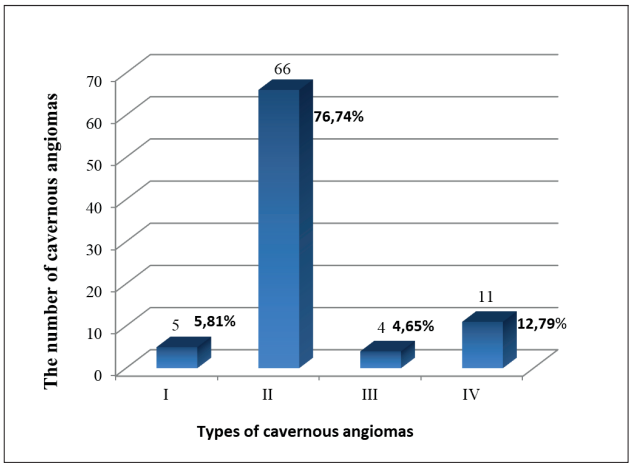

Figure 3. The frequency of the types of cavernous angioma analysed, with a diameter ≥3mm, according to Zabramski's classification

	Types of cavernous angiomas (n)					
Gender	Type	1	Type2	Type3	Type4	Total
Men	3	34	3	8	48	
Women	2	32	1	3	38	
Total	5	66	4	11	86	

Table 1. Distribution of types of cavernous angioma by gender

with a diameter of <3mm. In five patients, alongside a CA with a diameter of ≥3mm, multiple CAs were confirmed (5 or more CAs) which were <3mm (90 CAs with a diameter <3mm), which were mainly visualized on T2W gradient echo sequence. Of the total of 66 subjects, in 53 (80.3%) subjects one CA each was confirmed, whilst in 13 subjects (19.7%), two or more CAs were confirmed (Figure 2). In 5 (7.57%) subjects with multiple CAs, a total of 104 CAs were verified (5 ,6, 6, 8 and 79 CAs per subject). The largest number of CAs in one patient was 79.

Of the 86 CAs analysed, the largest number of them (66, that is, 76.7%) had the characteristics of Type 2 CAs, whilst the smallest number were equivalent to Type 3 (4, that is, 4.7%) (Figure 3 et 4,Table 1). Type 2 CAs were significantly ($p<0.0001$; $\chi^2 = 82.24$) more frequent than the other three types. Table 1 shows the distribution of individual types of CA in male and female subjects.

Of the 86 CAs which were ≥3 mm in diameter, 6 (6.98%) were not visualized on either T1W or T2W sequences, which means that the sensitivity of standard spin echo sequences was 93.02% , which was also the sensitivity of the T2W sequence. No significant difference was shown in sensitivity between spin echo sequences and T2W* ($p=0.87$; $\chi^2=0.028$) in the group comprising CAs with a diameter ≥3 mm. The sensitivity of the T1W sequence in the same group was 87.21%. No statistically significant difference was found in the sensitivity of T1W and T2W sequences ($p=0.85$; $\chi^2=0.032$), although according to the data in Table 2 it may be seen that on T2W, 77 (89.53%) CAs were well visualized, but on T1W, 56 (65.11%) CAs. Table 2 shows the visualization of cavernous angiomas on T1W and T2W sequences.

Of 104 CAs confirmed in subjects with multiple CAs, 90 were <3mm in diameter, whilst in subjects with one to four CAs, none of the CAs were < 3mm. Of 90 punctiform CAs, none was visualized on T1W sequence, and 10 CAs (11.11%) were

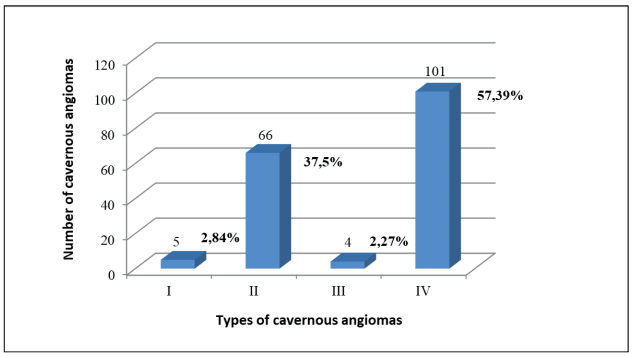

Figure 4. The frequency of the types of all cavernous angiomas visualized on spin echo and gradient echo sequences, according to Zabramski's classification

Sequence	Not visualized	Suspected CA	Well visualized	Total (n)
T1W	11	19	56	86
T2W	6	3	77	86

CA = cavernous angioma

Table 2. Visualization of cavernous angiomas on T!W and T2W sequences

visualized on T2W sequence as a punctiform absence of signal, which means that the sensitivity of T2W sequence, which is also the sensitivity of spin echo sequence, was 11.11%. In each group T2W* was significantly more sensitive than standard T1W ($p<0.0001$; $\chi^2=65.27$) and T2W sequence ($p<0.0001$; $\chi^2=43.075$). Only 30 (34.88%) of 86 CAs had a stronger signal post-contrast, without improvement of the visualization of the lesion in relation to the pre-contrast tomogram.

5. DISCUSSION

The exact prevalence of CA is unknown because many patients with CAs are asymptomatic, and never undergo radiological testing (CT or MR). In the study by Flemming et al. (2017), the prevalence of CAs in the population aged between 50 and 89 years was 0.46% (95% CI, 0.05-0.86)(4). In our research, in 66 (0.57%) of the 11,502 patients who underwent MR of the brain, one or more CAs were confirmed. A total of 86 CAs were verified and analysed that were larger than 3 mm, and a further 90 CAs with a diameter less than 3mm, in patients with multiple CAs. These results correlate with the results from the literature. The usual age of presentation of CAs is around the second decade of life, but there are also reported cases of CAs discovered in infants. As many as a hundred CAs may be found in one person, depending on the age of the patient and the mode of brain imaging (9). In the present study, the ages of the patients ranged from 1 to 78 years, with an average age of 47.68 ± 18.96. The smallest number of subjects were in the 20 to 30 years age group. The largest number of patients were in the 60 and 70 years age group, after which there was a drop in the frequency of CAs. These results do not differ significantly from the results obtained by Flemming et al., in that in their research the most CAs were verified in the group of patients aged between 50 and 59 years, and not between 60 and 70 years (4). There was no difference in the frequency of CAs between sexes, that is, the number of men and women was identical (33 people each). These results (50% men and 50% women with CAs) are identical to those obtained by Kang et al. (10). In this research, the highest number of subjects had one CA each. Of the total of 66 subjects, in 53 (80.3%) subjects one CA each was confirmed,

whilst in 13 subjects (19.7%), two or more CAs were confirmed. Five (7.57%) subjects were recorded with multiple Cas and they had a total of 104 verified CAs. The largest number of CAs per patient was 79, of which 42 were verified in the right and 37 in the left hemisphere of the brain. The results are similar to those obtained by Juri et al., in that their sample was significantly larger (11). In the present study, of 86 CAs that were ≥3mm there were most Type 2 CAs (76.7%), then 5.81% Type 1, 4.65% Type 3, and 12.79% Type 4 lesions. As in most other studies, the highest number of CAs were Type 2 (12, 13, 14). However, in the group of all the verified CAs (CAs ≥3mm and CAs <3mm), the largest number were Type 4, 57.39%, and only then Type 2, with 37.5% lesions, whilst the percentages of Types 1 and 3 CAs were almost equal (2.84% and 2.27%). These results are similar to those of Juri et al. (11). With the introduction of T2W gradient echo sequence, the frequency of Type 4 CAs increased in comparison with Type 2, in view of the fact that Type 4 CAs are usually punctiform and extremely difficult to visualize on spin echo sequences. Before the widespread use of MR, CAs were considered rare entities. Modern MR sequences are very sensitive for revealing CAs, as well as bleeding in various phases of thrombosis and reorganization (15). In the present study, the visualization was analysed of CAs on T1W, T2W spin echo and T2W gradient echo sequences. Of the 86 CAs which were ≥3 mm in diameter, 6 (6.98%) were not visualized on either T1W or T2W sequences, which means that the sensitivity of standard spin echo sequences was 93.02%. No significant difference was found in terms of sensitivity between spin echo sequences and T2W* in the group comprising CAs with a diameter ≥3 mm. No statistically significant difference was found in the sensitivity of T1W and T2W sequences, although on T2W, 77 (89.53%) CAs were well visualized, and on T1W only 56 (65.11%) CAs. Of 90 punctiform CAs, none was visualized on T1W sequence, and 10 CAs (11.11%) were visualized on T2W sequence as punctiform absences of signal, which means that the sensitivity of T2W sequence, which is also the sensitivity of spin echo sequence, was only 11.11%. In this group, T2W* was significantly more sensitive than standard T1W and T2W sequences, which is in agreement with the world literature reviewed. Only 30 (34.88%) of 86 CAs had a stronger signal post-contrast, without improvement of visualization of the lesion in relation to the pre-contrast tomogram. These results confirm the theory that T2W* sequence is the gold standard for diagnostics of CAs, especially in the case of punctiform, Type 4 CAs, which cannot be diagnosed by spin echo sequences, whilst spin echo sequences are very sensitive in the detection of CAs which have a diameter larger than 3mm, and only one third of CAs give a stronger signal post-contrast.

6. CONCLUSION

The prevalence of cavernous angiomas in the study was 0.57%, and men and women were equally represented. The number of cavernous angiomas per patient was between 1 and 79 ; the average diameter was 11mm, the most common type of cavernous angioma, ≥ 3mm, was equivalent to Type II, whilst the largest number of cavernous angiomas, regardless of the size and visualization on individual sequences, were equivalent to Type IV. No significant difference was found in sensitivity between spin echo sequence and T2W gradient echo sequence in the group comprised of cavernous angiomas ≥ 3mm, whilst in the group comprised of punctiform cavernomas < 3mm T2W* was a significantly more sensitive sequence than spin echo, that is, spin echo sequence had significantly lower sensitivity in the detection of punctiform CA.

- **Patient Consent Form:** All participants were informed about subject of the study.
- **Author's Contribution:** A.M, S.M, Z.M, N.M and R.H. gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. A.M, S.M, Z.M, N.M and R.H.had a part in article preparing for drafting or revising it critically for important intellectual content. A.M, S.M, Z.M, N.M and R.H. gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflicts of interest:** There are no conflicts of interest.
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