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Original Article

Fast three-dimensional time-of-flight magnetic resonance angiography: Should it be used in routine neuroimaging for headaches?

Kahraman Ahmet Nedim, Ahmet Vural

Department of Radiology, University of Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey

Address for correspondence:
Ahmet Vural, Fatih Sultan Mehmet Training and Research Hospital, E-5 Karayolu Uzeri, 34752 Atasehir, Istanbul, Turkey. Phone: +90-532-727-74-61. Fax: +90-216-575-04-06. E-mail: vuralahmet@gmail.com

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ABSTRACT

Objectives: We aimed to evaluate the diagnostic efficacy of fast three-dimensional (3D) time-of-flight (TOF) magnetic resonance angiography (MRA) in the detection of cerebral aneurysms.

Methods: We screened 1589 patients over a 3-year period, who underwent a magnetic resonance imaging for headache. Fast 3D TOF MRA images taken in addition to routine neuroimaging sequences, which were examined by two independent observers to assess cerebral aneurysms.

Results: Sixty-nine aneurysms were detected in 63 patients. The locations of the aneurysms were as follows: Middle cerebral artery, 27.5% (n = 19); internal carotid artery, 53.6% (n = 37); anterior cerebral artery, 5.8% (n = 4); posterior cerebral artery, 5.8% (n = 4); anterior communicating artery, 5.8% (n = 4); and ophthalmic artery, 1.4% (n = 1). Thirty-five (50.7%) were 7 mm or less, 23 (33.3%) were 8–10 mm, and 11 (15.9%) were 11 mm or larger. About 88% of pathological cases (n = 61) were saccular and 12 (n = 8) were fusiform type aneurysms. The interobserver compliance was high (K = 0.83) for detecting the aneurysms.

Conclusion: Considering the mortality and morbidity of subarachnoid hemorrhages, 3D TOF MRA is a successful, non-invasive method for detecting cerebral aneurysms. Results of the present study have shown that adding 3D TOF MRA to the routine brain imaging protocol is a beneficial tool for diagnosis.

Keywords: Magnetic resonance angiography, Intracranial aneurysm, Headaches, Neuroimaging

Introduction

The overall prevalence of intracranial aneurysms was found to be 2.85–9% in different series.[1,2] This high prevalence, combined with subarachnoid hemorrhage caused by the rupture of intracranial aneurysm, is the cause of high mortality and morbidity.[3,4] In a population study including 21 countries, the average incidence of subarachnoid bleeding secondary to the aneurysm rupture was found to be 9/100,000. However, this value varies among the countries and can be higher in Japan and Finland with the rates such as 22.7 and 19.7.[5]

Because of rapid advances in imaging techniques, the number of cerebral aneurysms detected by computed tomography (CT) angiography and magnetic resonance angiography (MRA) is increasing. The accuracy of MRA is over 90%, depending on the size of the aneurysm.[6,7] Those with a diameter of 5 mm or smaller are classified as small aneurysms and involve technical difficulties in neuroradiological evaluation. The use of traditional two-dimensional methods, the lack of innovative post-processing methods such as three-dimensional (3D), maximum intensity projection (MIP), and volume rendering (VR) limits the diagnostic accuracy of MRA.[8,9] However, the advancement in hardware and software of magnetic resonance imaging (MRI) scanners, along with the post-processing techniques and increased observer experience, leads to better diagnosis of small aneurysms due to increased sensitivity.[10] In this context, 3D time-of-flight (TOF) MRA has high sensitivity and specificity in detecting cerebral aneurysms, and publications indicating that it is possible to display aneurysms of 2–3 mm diameter and small vessels of 1 mm diameter.[3,4,6,7,11]

In this study, we aimed to demonstrate that the fast 3D TOF MRA could be a useful method in diagnostic procedures of patients with cerebral aneurysms due to its non-invasive nature and a high degree of accuracy and sensitivity. We aimed to discuss the benefits of adding 3D TOF MRA, which can be

performed in under a minute, to sequences used in routine brain MRI examinations.

Methods

The study consisted of 1589 patients who underwent a MRI examination to investigate the etiology of headaches over 3 years. Of the 1589 subjects evaluated, 809 were female (51%) and 780 were male (49%). The mean age was 43.12 (years) ± 19.3 (standard deviation) and the age range varied between 9 and 88 years [Table 1]. Sixty-nine cerebral aneurysms were detected in 63 patients with 3D TOF MRA. The aneurysm group consisted of 44 women and 19 men. The average age was 49.40 ± 18.02 (age range 11–82 years). The mean age for female patients was 48.80 ± 18.2 and 50.79 ± 18.1 for the male.

The study was approved by the Institutional Review Board and Ethics Committee, which conforms to protocols for human subject research in accordance with the Declaration of Helsinki (permission no 17073117-050.06). Written informed consents were obtained from all patients enrolled in the study.

Fast 3D TOF MRA images taken in addition to routine neuroimaging sequences in all patients were examined by two independent observers for the presence of cerebral aneurysms. Descriptive statistics were used for localization, size, number, type of aneurysms, and presence of thrombosed aneurysms.

Patients of both sexes, who were >18 and who had gone through an MRI imaging for headache were included in the study. The patients who had a history of vascular diseases, brain aneurysm, and subarachnoid hemorrhage or brain surgery were excluded from the study.

Cranial MRA examinations of all patients were performed with a 1.5 T MRI device (Signa Explorer, GE Medical Systems, USA). The cases were viewed with an 8 channel standard head coil (HD 8 channel NV Array, GE Medical Systems, USA).

Cases were examined with optimized 3D TOF MRA in addition to routine brain imagining sequences. In this technique, for the images taken in axial plan, time to echo (TR) was applied as minimum 3.1 ms, time to repeat (TR) as 20 ms, rotation angle as 20°, receiver bandwidth as 31.25 kHz, field of view as 22 cm, phase imagining area as 1.0 mm, section thickness as 2 mm, section number as 26, and matrix as 320 × 192, NEX 1. With these parameters, the scan time was approximately 54 s.

Images were transferred into the Advantage Workstation v4.6 system (GE Healthcare, Turkey), MIP and source images were evaluated together and intracranial aneurysm screening was performed. Localization, size, number, type of aneurysms, presence of thrombosed aneurysms, and accompanying vascular variations were evaluated in patients with aneurysms.

All cases were independently analyzed by two radiologists with 7 and 9 years of experience in neuroradiology. 3D TOF MR angiographic source images and MIP and VR image data created from images were used in the analysis. Posterior cerebral artery (PCA) including internal carotid artery (ICA), anterior cerebral artery (ACA), anterior communicating artery (ACoA), middle cerebral artery (MCA) including M1-2 segment, ophthalmic artery, and vertebral and basilar arteries were included in the analysis. The largest diameter of the aneurysms detected in these regions measured and the size of the aneurysm was determined.

Statistical analysis

IBM SPSS Statistics software v.22 (IBM SPSS, Turkey) was used for the analysis. The results were shown using mean and standard deviation, percentage, median, minimum, and maximum for the descriptive statistics. Interobserver reliability was investigated by the Kappa test.

Results

In our study, 69 cerebral aneurysms were detected in 63 patients. The aneurysm group was composed of 44 women (69.8) and 19 men (30.2%) and had an average age of 49.40 ± 18.02 (age range 11–82 years). The mean age of female patients was 48.80±18.2 and mean age of male patients was calculated as 50.79 ± 18.1 [Table 2]. We observed that 20 of the patients with intracranial aneurysms were 39 years of age and under (29%), 31 were between 40 and 59 years of age (44.9%), and 18 were 60 years of age and over (26.1%).

Sixty-nine intracranial aneurysms detected in 19 (27.5%) were found MCA located, 37 (53.6%) ICA located, 4 (5.8%) ACA located, 4 (5.8%) PCA located, 4 (5.8%) ACoA located, and 1 (1.4%) ophthalmic artery located [Table 3].

In our study, 35 (50.7%) of aneurysms were measured at 7 mm and below, 23 (33.3%) were measured at 8–10 mm, and 11 (15.9%) were measured at 11 mm and above [Table 4].

Thrombosed aneurysms were detected in 5.8% (4 cases) of 69 patients with intracranial aneurysms. Of the 69 cases with

Table 1: Demographic data of subjects

Gender	Number of patients (*n*)	Percentage of patients (%)	Mean age±SD
Female	809	50.9	44.63±19.8
Male	780	49.1	41.56±18.4
Total	1589	100	43.12±19.3

Table 2: Demographic data of patients with aneurysm detection

Gender	Number of patients (*n*)	Percentage of patients (%)	Mean age±SD
Female	44	69.8	48.80±18.2
Male	19	30.2	50.79±18.1
Total	63	100	49.40±18

Table 3: The location of aneurysms

Location	Number (*n*)	Number (%)
Internal carotid artery	37	53.6
Middle cerebral artery	19	27.5
Anterior cerebral artery	4	5.8
Posterior cerebral artery	4	5.8
Anterior communicating artery	4	5.8
Ophthalmic artery	1	1.4
Total	69	100

Table 4: The size of aneurysms

Size	Number (*n*)	Percent
7 mm and below	35	50.7
8–10 mm	23	33.3
11 mm and above	11	15.9
Total	69	100

an aneurysm, 88% (61 cases) had a saccular aneurysm and 12% (8 cases) had a fusiform type aneurysm [Figures 1 and 2].

Sixty-one of the 69 aneurysms detected by observer 1 were detected by Observer 2, and all 61 aneurysms detected by Observer 2 were reported by Observer 1. Eight aneurysms detected by Observer 1 were not reported by Observer 2. The consensus was reached in 1520 patients who were considered to have no aneurysms by both observers. A Kappa test was conducted to evaluate the compatibility between the observers, and Cohen's kappa coefficient was 0.83 and it was concluded that the agreement between the two observers was high.

Discussion

The International Study of Unruptured Intracranial Aneurysms has shown that the location and size of non-ruptured cerebral aneurysms, found coincidentally, predict future risk of rupture.[12-14] Therefore, neuroimaging is critically important in the evaluation and treatment of patients with brain aneurysms. Each neuroimaging technique has its strengths and weakness. Three main imaging methods used for neuroimaging of cerebral aneurysms are CT angiography, MRA, and digital subtraction angiography.

The most important feature that distinguishes MR angiography from other angiographic methods is that contrast angiography, based on an exogenous contrast agent, which can also create an angiographic image without the need for a contrast agent. Under this circumstance, the physiological current creates the signal and image. TOF MRA and phase-contrast MRA are traditional unenhanced angiographic methods used for many years. Contrast-enhanced MRA has widely been replaced with unenhanced MRA in many anatomical regions, because it can be obtained with higher signal/noise ratio, faster imaging, and less artifact rate with contrast angiography. Despite these

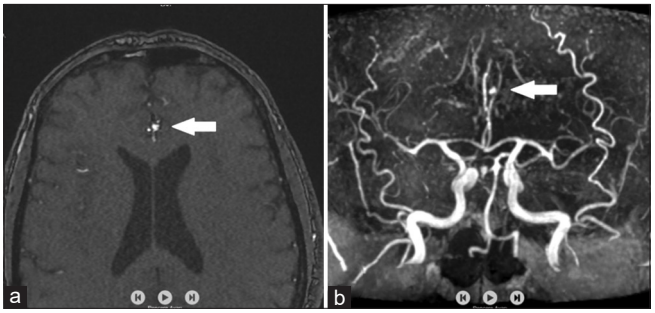

Figure 1: Magnetic resonance angiography (MRA) scan of aneurysms. (a) Axial time-of-flight (TOF) MRA demonstrates a left anterior cerebral artery aneurysm (arrow). (b) Three-dimensional TOF MRA clearly shows the pericallosal aneurysm (arrow)

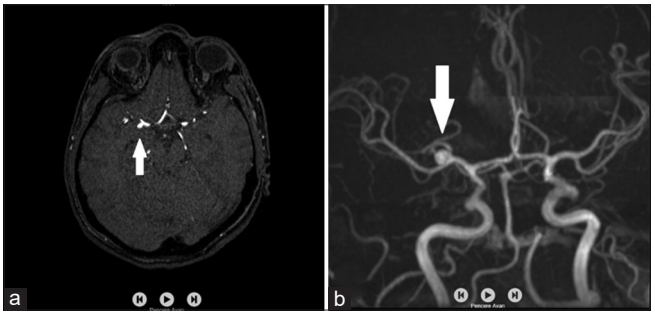

Figure 2: Unruptured right middle cerebral artery aneurysm. (a) Axial time-of-flight (TOF) magnetic resonance angiography (MRA) demonstrates a right middle cerebral artery aneurysm (arrow). (b) 3D TOF MRA demonstrating 6 mm blister aneurysm (arrow)

mentioned advantages, using contrast material also has a risk of adverse effects which can be as serious as the development of nephrogenic systemic fibrosis. Therefore, we reintroduced non-contrast MRA in parallel with the developments in MRI hardware/software.[15-18]

The previous studies have shown that 3D TOF MR angiography is highly sensitive (up to 95%) in the diagnosis of cerebral aneurysms greater than 5 mm; however, sensitivity for lesions smaller than 5 mm is limited.[8,9] In his study, Aprile reported that the sensitivity of MRI angiography in detecting cerebral aneurysms smaller than 3 mm (25%) was much lower than that of cerebral aneurysms larger than 3 mm (92%).[19] More recently, Hiratsuka *et al.* gave the susceptibility to aneurysm detection by 3D TOF MR angiography as 92% for aneurysms larger than 3 mm and 67% for aneurysms smaller than 3 mm.[7]

The training and level of experience of the observer is also another important factor for diagnostic accuracy. White *et al*. showed that the sensitivity and accuracy achieved by experienced observers were much higher than those achieved by less experienced observers.[20]

According to autopsy studies, the rate of non-ruptured coincidental intracranial aneurysms varies between 7% and 9%. Approximately 28,000 cases of subarachnoid hemorrhage due to ruptured aneurysm reported each year in the United

States, of which only 1/3 can survive without sequel. For these reasons, intracranial aneurysms and subarachnoid hemorrhage, which are the most common complication of aneurysms, considered to be a health problem that requires attention.[3,4]

In various studies, the frequency of random, non-bleeding intracranial aneurysms detected in the MRA examination was reported in the range of 2.8–5.1%. It has been shown in autopsy and angiographic studies that intracranial aneurysms are up to 66% more frequent in women.[3,21-24]

In some studies; 11–39% of aneurysms were ICA located, 4–15% were ACA located, 12–30% were ACoA located, 24–42% were MCA located, 3–13% were PComA located, and 4–12% were vertebral artery located.[25-28] In our study; of 69 detected intracranial aneurysms, 27.5% (n = 19) were found MCA located, 53.6% (n = 37) ICA located, 5.8% (n = 4) ACA located, 5.8% (n = 4) PCA located, 5.8% (n = 4) ACoA located, and 1.4% (n = 1) ophthalmic artery located.

In our study, thrombosed aneurysms were pointed out in 5.8% (four cases) of 69 patients with intracranial aneurysms.

Jeon *et al*.'s study found that 93% of aneurysms were smaller than 7 mm and 7% were larger than 7 mm or 7 mm.[21] In the study of Horikoshi *et al*., 95% of aneurysms were found to be smaller than 10 mm and 5% to be bigger than 10 mm.[24] In the study of Kaya *et al*., 73 (74.5%) of total 98 aneurysms found in 87 cases in which aneurysm is detected which were smaller than 7 mm; 15 (15.3%) of them were between 7 and 10 mm; and 10 (10.2%) were measured as 10 mm or bigger.[23] In our study, 50.7% (n = 35) of the aneurysms were measured at 7 mm and below, 33.3% (n = 23) were measured at 8–10 mm, and 15.9% (n = 11) were measured at 11 mm and above.

In the study of Jeon *et al*., 57.6% of aneurysms were found between the ages of 60 and 79; in Kaya *et al.*'s study, 45% of those diagnosed with aneurysms were between the ages of 40 and 59 and 39% were between the ages of 60 and 79.[25,27] Our study shows that 29% (n = 20) aged 39 and below, 44.9% (n = 31) aged 40–59, and 26.1% (n = 18) aged 60 and above.

The blood flow of the ACoA, which acts as collateral between bilateral ACAs, is under the effect of pressure difference of the ICAs. If the pressure is not equal in the A1 segments of the ACA, the current in ACoA gets affected. Therefore, the asymmetry in ACA proximal segments increases the incidence of ACoA aneurysms.[25] In some studies, it was reported that ACA A1 segment hypoplasia or agenesis was accompanied in 50–85% of cases with ACoA aneurysm.[26-28] In our study, ACA A1 hypoplasia observed in two out of four patients with an aneurysm in ACoA [Figure 3].

Of the 69 cases involving aneurysms, 61 (88%) involved saccular aneurysms; 8 (12%) involved fusiform type aneurysms.

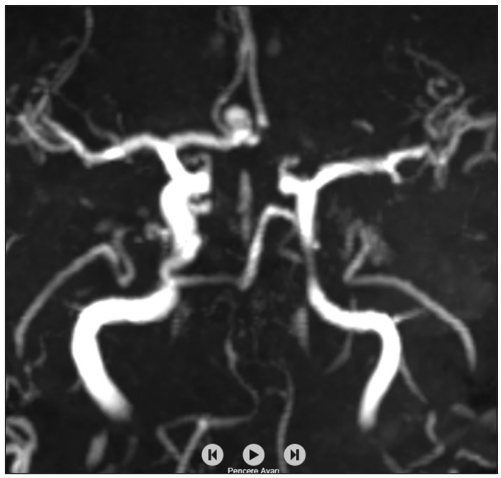

Figure 3: Anterior cerebral artery hypoplasia with anterior communicating artery aneurysm

Published data showed that the aneurysm site is one of the main factors affecting its detection. False-positive results for aneurysm were detected in areas with ACoA, anterior choroidal artery, ophthalmic artery, and other small branches from the ICA. An infundibulum in the mentioned area may mimic a small aneurysm because the origin of the vessels is too curved, overlapping, or if the vessel is connected to at the top of the infundibulum cannot be displayed.[7,9]

Some previous studies seem to have low rates in detecting cerebral aneurysms. When the methods of these researchers are analyzed, it is seen that they use MR imaging systems with outdated technology. It is also seen that these researchers used suboptimal MR angiography parameters and did not use VR images.[29] Due to the various signal densities produced by turbulence, calcification, and intraluminal thrombus, which could show high signal density on T1-weighted images, a confusing variability can be seen in signal densities on MRI images of aneurysms. Such factors appear to be less effective in 3.0 T reviews than in 0.5–1.5 T reviews. In addition, small aneurysms can often be misinterpreted in MIP images. False-positive diagnosis may occur due to vascular branching, overlapping images, atherosclerotic plaques, turbulent flow, or some combination of these.[29-31]

In clinical practice, we see that a large number of brain MRI examinations are performed, especially due to headache. A total of 12,509,470 MR examinations were performed in Turkey during 2018, of which 3,225,090 were reported to be brain MRI examinations.[32] The possibility of significant pathology is very low, especially as a result of brain MRI examinations due to headache.[33] In this study, we aimed to determine the value of additional information that can be obtained with fast 3D TOF MRA, which takes less than 1 min to be added to routine brain MRI examinations, as large numbers of examinations are in question. Our main goal in our study was not to compare the success of 3D TOF MRA or to reveal its missing aspects. For this reason, patients were evaluated only by 3D TOF MRA examination and could be considered as limiting side of our

study in terms of suspicious cases and in terms of missing small aneurysms. Digital subtraction angiography (DSA) is recognized as the gold standard for the diagnosis and pre-operative evaluation of intracranial aneurysms. The fact that DSA carries risks such as thromboembolism, contrast agent reactions, nephrotoxicity and is a relatively invasive method sometimes creates difficulties in practice. In addition, after subarachnoid hemorrhage, the patient's condition is often critical and it is difficult to apply DSA. In parallel with the developing technology, intensive studies have been carried out on non-invasive diagnostic methods in recent years. [3,4,9,11], and it also most of the patient is in a serious condition after subarachnoid hemorrhage and not shifting toward invasive diagnostic methods in recent years, and evolving technology has led to focus their studies in parallel with other diagnostic methods.[3,4,9,11] The results of the study were close and consistent with those reported in the literature. Our findings also support the idea that the technology available for 3D TOF MR angiography can safely replace intra-arterial DSA in the diagnostic procedures of patients with cerebral aneurysms, as have been reported in the previous studies.[34]

With the extensive database that will be formed using 3D TOF MRA in routine neuroimaging, we can assume that much more information can be obtained in the future about its nature, types, behavior, and risks of cerebral aneurysms. Thus, we assume that removing the mortality and morbidity that subarachnoid hemorrhage caused will advance.

Conclusion

As a result, radiological studies are showing the overall prevalence of intracranial aneurysms between 2.8 and 5.1%, and autopsy studies showing the range of 7–9%. However, subarachnoid hemorrhage caused by torn intracranial aneurysm is a devastating condition associated with high mortality and morbidity despite advances in treatment. For the above-mentioned reasons, intracranial aneurysms and subarachnoid hemorrhage, which are the most common complication of aneurysms, are considered to be a health problem that must be taken into consideration.[3,4] Fast 3D TOF MR angiography shows high diagnostic accuracy in the detection of cerebral aneurysms. In conclusion, we suggest that 3D TOF MR angiography is a highly successful method in diagnostic procedures of patients with cerebral aneurysms because its quick (can be done in a minute), non-invasive, and is highly sensitive and specific. Thus, it would be useful to add 3D TOF MRA to sequences used in routine neuroimaging.

Authors' Declaration Statements

Ethical approval

The study was approved by the Institutional Review Board and Ethics Committee (University of Health Sciences, Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey), which conforms to protocols for human subject research in accordance with the Declaration of Helsinki (permission no 17073117-050.06).

Availability of Data and Material

The data used in this study are available and will be provided by the corresponding author on a reasonable request.

Competing Interest

The authors declare none.

Funding Statement

No funding was received for the study.

Authors' Contributions

All the authors have equally contributed in every stage in the preparation of this manuscript.

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ORCID link of the corresponding author

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