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DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE ANGIOGRAPHY FOR UNRUPTURED CEREBRAL ANEURYSMS IN CORRELATION WITH DIGITAL SUBTRACTION ANGIOGRAPHY

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Intracranial aneurysm is a focal, abnormal dilation of an artery of the brain. Magnetic resonance angiography (MRA) is a non-invasive technique for vascular imaging and is thus widely used for screening for intracranial vascular lesions. The aim of the study was to show the diagnostic accuracy of 3D Time-of-Flight (3D TOF) MRA in the detection of unruptured cerebral aneurysms with the use of digital subtraction angiography (DSA) as the gold standard. A total of 2.612 consecutive patients underwent 3D-TOF MRA. It showed unruptured aneurysms in 94 (3.6%) patients. They included 68 women and 26 men ranging in age from 29 to 76 years (mean, 52.5 years). Twenty-six of them, 20 women and 6 men, underwent DSA. The Mann-Whitney U test was used for the correlation of size. Fisher's test was used for the correlation of location. The statistical level of significance was set at $p<0.05$. Most often, the aneurysms were located in the bifurcation of the middle cerebral artery (MCA, n=28, 33.33%) and the internal carotid artery (ICA, n=16, 19%). The mean size of aneurysms was 5.4 mm (range 2 - 15 mm). There was no statistically signifficant difference in the detection and the location ($p=0.732$) as well as the size ($p>0.05$) of aneurysms between TOF MRA and DSA.

MRA is an accurate and non-invasive method for diagnosis of unruptured intracranial aneurysms. The results of study show the compatibility of MRA findings, the location and the size of an aneurysm in comparison with the "gold standard" - cerebral DSA. *Acta Medica Medianae 2015;54(3):12-18.*

***Key words**: intracranial unruptured aneurysm, magnetic resonance angiography, digital subtraction angiography*

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Introduction

Intracranial aneurysm is a focal, abnormal dilation of an artery of the brain caused by the weakness in the innermost layer of the arterial wall, called the intima. Aneurysms are most commonly localized in the subarachnoid space at the base of the brain. The four major types of intracranial or cerebral aneurysms include: saccular, fusiform, dissecting, and micotic type. The most common type is the saccular aneurysm which accounts for 90% of all intracranial aneurysms and they most often occur at the branch points of arteries of the circle of Willis (1).

The pressure existing within the arterial blood vessel leads to aneurysm growth i.e. to a gradual appearance of a bulge in the wall of an artery which can gradually become thinner and eventually burst. The result of this rupture is a subarachnoid hemorrhage (SAH), which is clinically manifested by severe headache ("the worst in life") that may or may not be accompanied by nausea, vomiting, stiff neck and neurological changes (2).

However, unruptured aneurysms are usually asymptomatic. Only 10-15% of intracranial aneurysms display symptoms such as a severe headache, bilateral temporal hemianopsia, unilateral third cranial nerve palsy and poorly defined spells and seizures (3-5).

Among the several imaging modalities commonly used in the diagnosis of an intracranial aneurysm, digital subtraction angiography (DSA) is still considered the gold standard. However, since DSA is an invasive method, it can be associated with a very low, but still possible risk of morbidity (6).

Several other non-invasive imaging methods such as computed tomographic angiography (CTA) or magnetic resonance angiography (MRA) have been developed and are now widely used for the detection and assessment of aneurysms and vascular pathology.

MRA enables a faster and non-invasive detection of aneurysms, and is nowadays used in routine clinical practice. Due to recent advances, the quality of the images obtained by these non-invasive imaging methods has been significantly improved, which provides higher sensitivity and more accuracy. Apart from the precise detection of an aneurysm, this also enables obtaining more valuable information regarding the shape, the size as well as the hemodynamic flow characteristics of intracranial aneurysms (7, 8).

Therefore, MRA is widely used as an imaging technique for the screening of intracranial vascular lesions.

The presence of an unruptured aneurysm is not uncommon. The reports about intracranial aneurysms in the general population show that prevalence is 1%-9% in autopsy series and 0.5%-2% in imaging studies (4, 9, 10).

Due to recent advances in non-invasive imaging techniques, the accuracy of the diagnosis of an unruptured intracranial aneurysm has significantly increased. This also resulted in incidental asymptomatic aneurysms becoming a substantial clinical burden as their natural history is controversial (10).

The aim of the study was to show the diagnostic accuracy of 3D Time-of-Flight (3D TOF) MRA in the detection of unruptured cerebral aneurysms with the use of digital subtraction angiography (DSA) as the gold standard.

Materials and methods

The retrospective study included 94 patients who underwent MRI with MRA in whom intracranial aneurysms were detected incidentally in the period between January and December 2014. None of the patients had the symptoms of SAH. All the examinations were performed at the Center for Radiology, Clinical Center Nis on 1.5-T MR (Avanto Siemens, Erlangen, Germany). According to the protocol, TOF MRA with multiplanar reconstruction was performed in all of the patients suspected with the existence of intracranial aneurysm. MRA was performed in 2.612 people, and in 94 patients (3.6%) an aneurysm was detected.

Three-dimensional time-of-flight magnetic resonance angiography technique was used with imaging parameters of 23/7.15 (TR/TE) and ramped pulse from 15 to 25 with a centre flip angle of 20. The whole volume was divided into 7 slabs with 8 slice oversampling. Each slab consisted of 52 slices, resulting in slice thickness of 0.80 mm. The overall vessel coverage with this technique was 230 mm (FOV read). It was placed to include the structures from foramen magnum to distal branches of intracranial arteries.The diagnosis of an aneurysm was performed after evaluating the maximum intensity projections (MIP) images and individual axial sections.

The average age of the patients with aneurysms was 52.5±23.5 years, most of them presented in the 5th decade, the youngest of whom was 29 and the oldest 76 years old (Table 1). MRA examination was performed in 68 women (68/94, 72.34%) and 26 men (26/94; 27.66%) (Table 2).

Table 1. The age of the examined population

	Mean±SD	Min-Max
Age	52.5 ± 23.5	29.00-76.00

In case an aneurysm was detected, its location and size were determined.

In 26 patients with an aneurysm detected by TOF-MRA, a DSA of cerebral arteries was performed using a DSA unit (Siemens Axiom Artis, Erlangen, Germany), with a standard Seldinger technique using 5F sheath and catheter systems. A catheter was positioned at the cervical portion of the carotid arteries and vertebral arteries, and a dose of 6 to 9 mL of the contrast medium (Ultravist, 370 mg/mL) was injected at a rate of 3 to 4 mL/s. A three-dimensional (3D) reconstruction algorithm based on the algebraic reconstruction technique automatically produced 3D subtraction images on the workstation.

Cerebral DSA was performed in twenty women (20/26, 76.92%) and six men (6/26; 23.07 %) (Table 2). The location and the size of aneurysms were analyzed on angiograms. The MRA findings were compared with those of cerebral DSA.

Table 2. The gender of the examined population in whom the aneurysms were detected

	MRA		DSA	
Gender	N	%	N	%
Female	68	72.34	20	76.92
Male	26	27.66	6	23.07

The absolute numbers and their percentage structure were used for showing the frequency. The Mann-Whitney U test was used for the comparison of the aneurysm size. The comparison of frequency was performed by Fisher's exact probability test. The statistical level of significance was set at $p<0.05$. The statistical analyses were performed using the software package SPSS (version 15).

Results

The TOF-MRA examinations included 94 patients with aneurysms and have shown that an aneurysm is most often located at the bifurcation of the medial cerebral artery (MCA) as detected in 28 of the examined patients (33.33%). In 16 patients the aneurysm was detected in C1 segment of the internal carotid artery (ICA) (19%). No aneu-

Table 3. The distribution of incidental unruptured aneurysms

	MRA		DSA	
Localization	N	%	N	%
C3 segment ICA	4	4,7	2	7,69
C2 segment ICA	8	9,52	2	7,69
C1 segment ICA	16	19,05	4	15,38
Bifurcation ICA	4	4,76	4	15,38
A1 segment ACA	0	0	0	0
ACoA	10	11,90	2	7,69
M1 segment MCA	10	11,90	2	7,69
Bifurcation MCA	28	33,33	6	23,08
VA	2	2,38	0	0
PICA	6	7,14	2	7,69
BA	6	7,14	2	7,69

rysm was detected in A1 segment (Table 3).

In 26 patients in whom the TOF MRA revealed an aneurysm, DSA cerebral angiography was performed and the findings have again shown that the highest incidence of aneurysms occurs at the MCA bifurcation (6/26; 23.07%) (Table 3).

The most common location of the aneurysms, as determined by MRA, was at the bifurcation MCA (28/94 or 33.3%). DSA has also revealed that the most common sites of aneurysms are at the bifurcation MCA (6/26 or 23.07%; Fisher: p=0.732) (Table 3).

In the posterior cerebral circulation, the number of the detected aneurysms was smaller, with a higher incidence of aneurysms in the basilar artery, as seen on both MRA and DSA (Table 3).

The results of our study have clearly showed that there was no statistically significant difference in the location of aneurysms detected by MRA and those detected by DSA.

Furthermore, the exploration of the distal parts of intracranial blood vessels was carried out, using both methods, and no aneurysmal and steno-occlusive lesions nor arteriovenous malformations (AVM) were found. The explored blood vessels did not show any signs of spasm.

Further analysis was carried out by the comparison of the results obtained by TOF MRA and DSA cerebral angiography.

Table 4. The mean value of size of unruptured aneurysms detected by both techniques

	Mean±SD	Min-Max
Size of aneurysm mm (MRA, DSA)	5.4±1.8	2.00-15.00

In 26 patients who underwent both methods, no statistically significant difference was found in the size of the aneurysms (p>0.05). The largest aneurysm measured 15 mm, and the smallest 2 mm (Table 4).

Discussion

Intracranial aneurysms are common in the general population with the reported prevalence of 3.6 percent, predominantly in women. A ruptured aneurysm is considered to be the main cause of a non-traumatic SAH. Seventy-seven percent of cases of SAH are due to an aneurysmal rupture. The incidence of intracranial aneurysm rupture is approximately 12/100.000 population/year (11-13).

There are usually no symptoms caused by an unruptured aneurysm. The symptoms occur when aneurysms rupture or if they cause a compression of the adjacent neural structures which results in focal neurological deficits (6).

A decrease in the middle muscular layer of an artery, the tunica media, which causes a structural deficit, represents the most usual histological finding. Together with hemodynamic factors, these structural defects cause outpouchings at major intracranial branch points in the subarachnoid space located at the base of the brain (14).

It is not possible to predict who among the general population has an aneurysm and whether it will bleed, but it is possible to single out groups with an increased risk (polycystic kidney disease, Ehlers Danlos syndrome, Marfan syndrome, family history of aneurysms in close relatives, patients who have already been diagnosed with an aneurysm). Screening among these vulnerable population groups, given that the treatment of aneurysms detected in this manner has a lower mortality and morbidity rate, could save many lives (1, 15).

The occurrence of aneurysms is conditioned by several factors - genetic predisposition is combined with secondary risk factors which causes the formation of lesions of a blood vessel wall. Ninety-five percent of all aneurysms are caused by congenital predisposition and atherosclerotic changes (hypertension and smoking being the main risk factors) (6).

The most common intracranial aneurysms occur in four basic types: saccular, fusiform, dissecting, and micotic type. Aneurysms most commonly occur in an elderly population. The clinical symptoms of aneurysm usually start between 40 and 60 years of age. Intracranial aneurysms are very rare in children, only 2%. The incidence of aneurysms in boys is higher than in girls, and this ratio is 3:1. Approximately, 20% of all aneurysms in children are diagnosed in the last segment of the circle of Willis or in the distal vessels (17).

There has been a significant increase in the incidental detection of unruptured intracranial aneurysm due to the recent advances in the imaging techniques and the common use of noninvasive imaging methods such as CT or MR angiography (18). Since there is no exposure to radiation nor the iodinated contrast agent is used, MRA may be the method of the first choice for the screening setting (19).

MRA is a fast, accurate and non-invasive method for the detection of aneurysms with none of the risks that may be involved in the conventional angiography.

Since the aneurysms may overlap with adjacent arteries and the signal is reduced by the flow patterns, the detection of small (5-7 mm) or very small (<3 mm) aneurysms on maximum-intensity-projection images can often be difficult (20-22).

A sensitivity of detection of untreated aneurysms by the use of MRA, as shown by the recent studies, is up to 96.7%, which is comparable with that of DSA (23-25).

Based on the comparison of 3 T with 1.5 T 3D TOF MRA, in their study, Willinek et al. (26) concluded that an improved spatial resolution as well as better evaluation of the peripheral segments of intracranial vessels are obtained by 3 T.

The optimal vascular contrast is provided by TOF MRA sequences.

2D TOF technique is sensitive to slow flow, and it provides an excellent background suppression. The images obtained by this technique are in the axial plane, perpendicular to the direction of the blood vessels (Fig.1.a). The images in 3D TOF technique are obtained by the application of a 3D volume (slab) oriented perpendicular to the direction of flow which produces an enhanced flow and affects only the spins included in the acquired slab (Figure 1.b,c) (27).

TOF MRA technique has an excellent spatial resolution and it enables the analysis of all larger intradural arteries at the base of the brain. However, MRA has not yet replaced the conventional catheter cerebral angiography. The accuracy of MRA depends on how many of the images are processed and reviewed (28).

Aneurysm screening is still a matter of debate. However, for high-risk populations, due to a family history of intracranial aneurysm or patients diagnosed with polycystic kidney disease who thus have a higher risk of aneurysms, the screening is generally accepted.

Since MRI is a procedure for diagnosing a large number of potential pathologies such as stroke, neurologic dysfunctions etc. each of these intracranial MRA examinations should also assess the potential presence of an aneurysm (29).

However, a slow blood flow within 3 mm aneurysms or smaller ones can result in possible missing to detect them with MR angiography. Furthermore, false positive and false negative interpretations can often be caused by a loop formation or a possible overlap of blood vessels. Due to a turbulent flow and a complex anatomy of the carotid siphon, the aneurysms located in that region are most likely to be missed (30).

Cerebral angiography is an invasive radiological technique used for the diagnosis of the blood vessels in the brain. This method is considered the gold standard for the diagnosis of aneurysms. The method consists of the injection of iodinated contrast in the carotid or vertebral artery, while at the same time an X-ray of the skull is performed. The method allows an accurate representation of the intracranial vessels.

This method enables obtaining valuable and detailed information about the presence, location, and morphology of aneurysms. It also reveals the relationship of an aneurysm both with its parent and

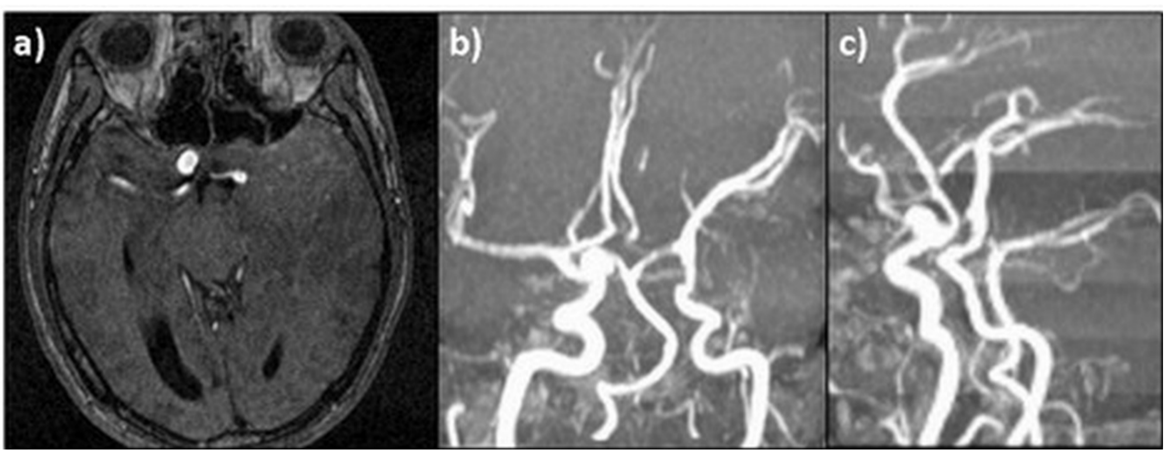

Figure 1. a) TOF MRA; b,c) 3D TOF MRA at the level of the circle of Willis shows an aneurysm in the C1 segment. This finding was confirmed by the DSA (Figure 2).

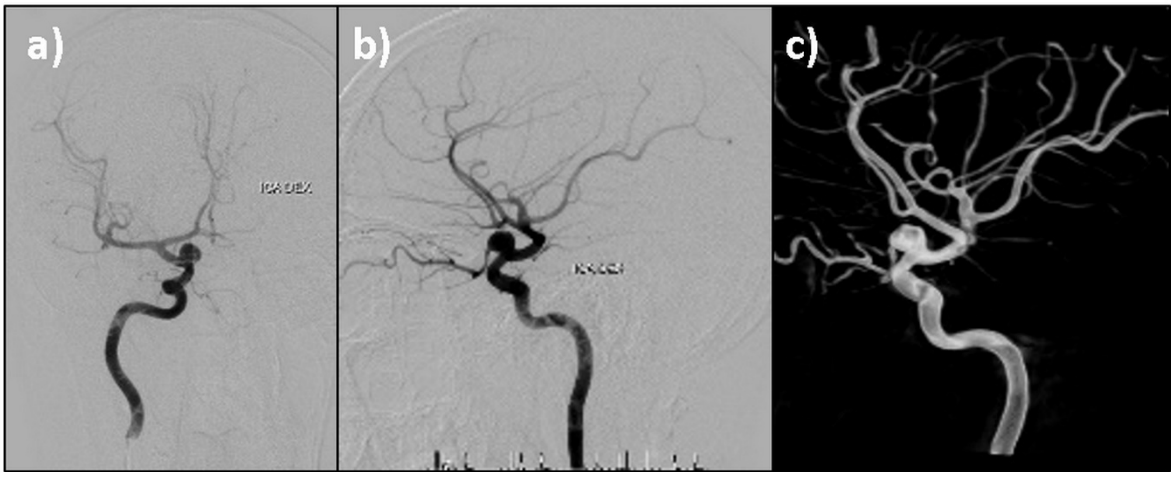

Figure 2. DSA angiograms in multi projections a) antero-posterior (AP); b) left lateral (LL); c) 3D in space angiograms show an aneurysm in the C1 segment of the internal carotid artery (ICA), in the same patient in whom an aneurysm has been previously confirmed by MRA (Figure 1).

adjacent vessels, and it also enables obtaining important information about aneurismal flow dynamics (31). Moreover, by introducing flat panel detector (FPD) technology, the image quality has been significantly enhanced and there has been a great reduction in radiation doses. The important features of FPD technology include high spatial resolution, wide dynamic range, and realtime imaging capability. The use of FPD technology enables a safer method of obtaining more rotational angiographic data as well as the creation of high-resolution 3D DSA images (Fig.2.c).

Standard anteroposterior, lateral and oblique projections are are most commonly used (Fig.2. a, b). The examination of renal function and coagulation factors in all patients is a requirement for angiography. The aim of the treatment is to exclude aneurysms from the circulation (32).

In our study, MRA revealed incidental aneurysms in 94 patients. The presence of all of the aneurysms was confirmed by cerebral DSA. The most common location of aneurysms on MRA and on DSA was at bifurcation MCA and in C1 segment of ICA. MRA and cerebral angiography provide identical findings with regard to aneurysm location.

The size of an aneurysm is an essential factor for the sensitivity of this method. MRA study is precise for revealing aneurysms larger than 5 mm (95.3%), but is less precise for smaller aneurysms. For the aneurysms smaller than 5 mm, the detection rate is 72.2 % (33).

However, these aneurysms must not be ignored despite their low rupture risk.

The largest aneurysm in our study measured 15 mm. The smallest aneurysm detected in our study had a diameter of 2 mm. By comparing the two methods, no statistically significant difference was found in the assessment of the size of aneurysms ($p>0.05$).

Conclusion

MRA is a modern, accurate and non-invasive method used for the detection of asymptomatic intracranial aneurysms. The results of our study show the compatibility of MRA findings, the location and size of an aneurysm in comparison with the "'gold standard" - cerebral DSA.

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KOMPARACIJA MAGNETNE REZONANTNE ANGIOGRAFIJE SA DIGITALNOM SUPTRAKCIONOM ANGIOGRAFIJOM U DIJAGNOSTIKOVANJU NERUPTURIRANIH INTRAKRANIJALNIH ANEURIZMI

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Intrakranijalne aneurizme predstavljaju fokalnu dilataciju krvnih sudova mozga. Magnetna rezonantna angiografija je neinvazivna tehnika koja omogućava prikaz krvnih sudova i ima primenu u skriningu intrakranijalnih vaskularnih lezija. Cilj rada bio je da se pokaže dijagnostička tačnost 3D Time-of-Flight (3D TOF) MRA u detekciji nerupturiranih cerebralnih aneurizmi u poređenju sa digitalnom suptrakcionom angiografijom (DSA) kao zlatnim standardom. Istraživanje je obuhvatilo 2612 bolesnika koji su bili podvrgnuti TOF MRA pregledu. Kod 94 (3,6%) bolesnika detektovano je prisustvo nerupturiranih aneurizmi i to kod 68 žena i 26 muškaraca, starosti od 29 do 76 godina (srednja vrednost 52,5 godina). Iz ove grupe je 26 bolesnika, 20 žena i 6 muškaraca, podvrgnuto DSA pregledu. Mann-Whitney U test je korišćen u korelacionoj analizi veličine aneuzmi, a Fischerov test u korelacionoj analizi lokalizacije. Nivo statističke značajnosti je određen vrednostima $p<0,05$. Najčešća lokalizacija aneurizmi bila je na bifurkaciji srednje cerebralne arterije (MCA, n=28, 33, 33%), a potom na unutrašnjoj karotidnoj arteriji (ICA, n=16,19%). Srednja vrednost veličine aneurizme bila je 5,4 mm (od 2 do 15 mm). Nije bilo statistički značajne razlike u detekciji i lokalizaciji (p=0,732), kao i u veličini ($p>0,05$) aneurizmi detektovanih TOF MRA i DSA pregledom. MRA je precizna i neinvazivna metoda u detekciji nerupturiranih intrakranijalnih aneurizmi. Rezultati studije pokazuju kompatibilnost između MRA nalaza, lokalizacije i veličine aneurizmi, u komparaciji sa zlatnim standardom—cerebralnom DSA. *Acta Medica Medianae 2015; 54(3):12-18.*

Ključne reči*: intrakranijalne nerupturirane aneurizme, magnetna rezonantna angiografija, digitalna suptrakciona angiografija*