ORIGINAL ARTICLE

Prospective Comparison of Multi-Detector Computed Tomographic Angiography with Digital Subtraction Angiography for the Diagnosis of Intracranial Aneurysms in Patients with Acute Non-Traumatic Subarachnoid Hemorrhage

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Abbreviations

ACA = anterior cerebral artery
ACoA = anterior communicating artery
BA = basilar artery
CTA= computed tomographic angiography
DSA = (intra-arterial) digital subtraction angiography
ICA =internal carotid artery
MCA = middle cerebral artery
PCA = posterior cerebral artery
SAH = subarachnoid hemorrhage

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ABSTRACT

BACKGROUND Rupture of intracranial aneurysms and malformations are the main causes of spontaneous subarachnoid hemorrhage (SAH). Multi-detector computed tomography angiography (CTA) and intra-arterial digital subtraction angiography (DSA) are used to evaluate cerebrovascular structures and to detect such abnormalities with an intention to treat them.

OBJECTIVE The aim of the present study was to compare CTA and DSA findings in the detection of a cerebral aneurysm in patients with acute non-traumatic SAH and to depict the diagnostic value of CTA.

METHODS During the last 3 years 52 patients with non-traumatic SAH were prospectively studied. Four patients underwent only 16-slice multi-detectorCTA and 48 patients underwent both CTA and DSA in an acute setting. Aneurysm morphologic information on CTA was compared to DSA, which is considered the gold standard imaging technique.

RESULTS The sensitivity of CTA per aneurysm was 97.9% (95% confidence intervals-CI 0.83-1), the specificity 100% (CI 0.50-0.99), the positive diagnostic likelihood ratio 0 and the negative diagnostic likelihood ratio 0.02. DSA successfully depicted 47 aneurysms in 40 patients from our study group. One aneurysm was missed on CTA (2mm) which retrospectively was identified. In 8 patients with SAH no aneurysm was detected by either CTA or DSA.

CONCLUSION 16-slice multi-detector CTA can be successfully used as a first choice imaging tool in the diagnostic algorithm of non-traumatic SAH and efficiently guide the therapeutic strategy.

INTRODUCTION

Subarachnoid hemorrhage (SAH) is a condition which is associated with high morbidity and mortality. Ruptured cerebral aneurysms are the commonest causes of non-traumatic SAH,[1] especially in women, where non traumatic SAH occurs 1.6 times more frequently than in men.[2] The prevalence of intracranial aneurysms varies between 1 and 5% in adults and in most cases remains asymptomatic.[3] The saccular type accounts for 90% of cerebral aneurysms and 85% of them occur in the circle of Willis.[4] In 20-30% of patients more than one aneurysm is detected by imaging.[5]

A good prognosis in patients with automatic non-traumatic SAH depends on the early detection of high risk individuals with hereditary conditions and strong clinical suspicion. The primary and adequate treatment with endovascular coiling or surgical clipping may reduce the risk of vasospasm and re-bleeding, which are the most important mortality factors.[6]

Intra-arterial digital subtraction angiography (DSA) is the gold standard method for detecting the existence of cerebral aneurysms[7] and for postoperative patient evaluation after surgical clipping of the aneurysm.[8] However, DSA is an invasive and expensive diagnostic procedure with a 0.07% rate of permanent neurologic deficits in patients with SAH and intracranial aneurysm.[9] Computed tomographic angiography (CTA) is an alternative non-invasive and inexpensive imaging procedure with the advantage of it being performed immediately after emergency unenhanced brain computed tomography in patients with SAH.[10] CTA is becoming the first choice for intracranial aneurysm detection in patients with SAH[11] and at some hospitals DSA has been replaced by CTA in preoperative planning and for patient follow up.[12,13]

The aim of our study was to evaluate the diagnostic value of CTA in comparison with intra-arterial DSA for the detection of intracranial aneurysms in patients with non-traumatic SAH.

PATIENTS AND METHODS

During the last three years 52 patients were admitted to our Emergency Radiology Department with clinical symptoms and signs indicating SAH and possible cerebral aneurysm rupture. The clinical presentation included generalized or localized severe headache, dizziness, impairment of extra-ocular movements, confusion and lethargy.

In all 52 patients the diagnosis of SAH was established by a cranial computed tomography scan. According to the World Federation of Neurosurgical Societies (WFNS) grading scale of SAH[14] the clinical status of the initial 52 patients was classified as follows: 17 patients grade I, 10 patients grade II, 3 patients grade III, 16 patients grade IV and 6 patients grade V. Fischer's classification, based on the total amount of intracranial blood, was grade II for 14 patients, grade III for 17 patients and grade IV for 21 patients.

All 52 patients with SAH underwent CTA. Forty-eight patients underwent both CTA and DSA. Four patients underwent only CTA due to clinical deterioration in two of them, refusal of one patient and known aneurysm in another patient from previously performed magnetic resonance imaging.

CTA was performed immediately after emergency unenhanced brain computed tomography scan, while DSA was performed within the first 6-24hours of diagnosis. Treatment planning was decided according to the results of CTA and DSA.

A selective four-vessel DSA via common femoral artery catheterization was carried out on an angiography unit (Integris V5000; Philips, Eindhoven, Holland) by two experienced interventional neuroradiologists. Anteroposterior, lateral and oblique views were routinely obtained to clarify the anatomy of the aneurysm. The total amount of non- ionic contrast media used was calculated according to body weight (1ml/kg) and ranged between 60ml and 120ml. The field of view was usually 20 cm and the matrix size was 1024x1024.

The CTAs were performed on a 16-row multislice computed tomography scanner (Aquilion TSX 101A; Toshiba Medical systems, Otawara, Japan). The scanogram included the area between the level of foramen magnum up to the cranial vault. A total volume of 80-100 ml of non-ionic contrast medium was injected intravenously at a rate of 4 ml/s by a power injector (Vistron CT injection system; Medrad, Indianola, USA). A bolus tracking method was used (triggering) with a threshold of 150 HU and the region of interest (ROI) was placed within the internal carotid artery. The scanning parameters were 120 KV, 300 mAs, speed 1sec/cycle, slice thickness 0.5 mm and pitch 2.

There were no allergic reactions noted. An informed consent was obtained from all patients or their legal representatives. Our protocol was approved by the Ethics Committee of Areteion Hospital.

The post processing was conducted by the use of a Vitrea workstation (Vitrea 2; Vital images, California, USA) by two experienced radiologists. MPR (multi-planar reformation), MIP (maximum intensity projections), SSD (surface shaded display), 3D hollow vessels and 3D VRT (volume rendered reconstruction) modes with 360^{o} rotation on the workstation were applied to each patient's datasets.

In our diagnostic algorithm the axial CTA images were evaluated first. Afterward MIP, SSD and VRT images were compared with axial images. The combined study of these images in patients with multiple aneurysms was useful to detect the ruptured aneurysm in relation to the aneurysms' morphology and hemorrhage distribution. The VRT and hollow vessel's images were helpful for more morphological details pertaining to the shape and neck of the aneurysm and its relationship to adjacent vessels. Aneurysm dimensions were measured on the MPR and 3D images.

The evaluation criteria of an aneurysm in CTA and DSA images included number, size, location, direction, shape, visualization/measurement of the aneurysm neck and presence of intramural thrombi, vasospasm and normal vascular variants.

Statistical analysis was carried out with Microsoft Office Excel as well as the Simple Interactive Statistical Analysis website which calculates indicators of diagnostic test effectiveness (SISA). Our sample space therefore focuses on the aneurysms and not the patients. The diagnostic likelihood ratio (DLR) is a valuable tool for comparing the accuracy of several tests to the gold standard method which is not dependent upon the prevalence of disease in contrast to the predictive value. The confidence intervals (CI) can also be calculated to reflect the statistical significance of each accuracy measure. Taking the DSA as the gold standard method in the detection of intracranial aneurysms, the sensitivity, specificity, positive and negative diagnostic likelihood ratio (DLR) of CTA were evaluated with 95% confidence intervals (CI).

RESULTS

Forty eight patients were included in our statistical analysis. In 8 of them both tests (CTA and DSA) were negative for the detection of intracranial aneurysms.

In the rest 40 patients 47 aneurysms were detected by using DSA images. Nineteen aneurysms were located in the anterior communicating artery (ACoA) with sizes ranging between 0.4cm to 1.5 cm (Fig. 1 a-d), 12 in the middle cerebral artery (MCA), 5 aneurysms left and 7 aneurysms right with sizes ranging between 0.2 cm and 2.5cm, 2 in the anterior cerebral artery (ACA) which were 0.4cm and 0.5cm ion size, 10 in the internal carotid artery (ICA), 8 aneurysms in the supraclinoid portion and 2 inthe cavernous portion with sizes ranging between 1 cm and 3.8 cm (Fig. 2 a-d), 2 in the posterior cerebral artery (PCA) which were 1.5cm and 2.5cm and 2 in the basilar artery (BA) with sizes 0.9cm and 1.1cm (Table). Six patients had

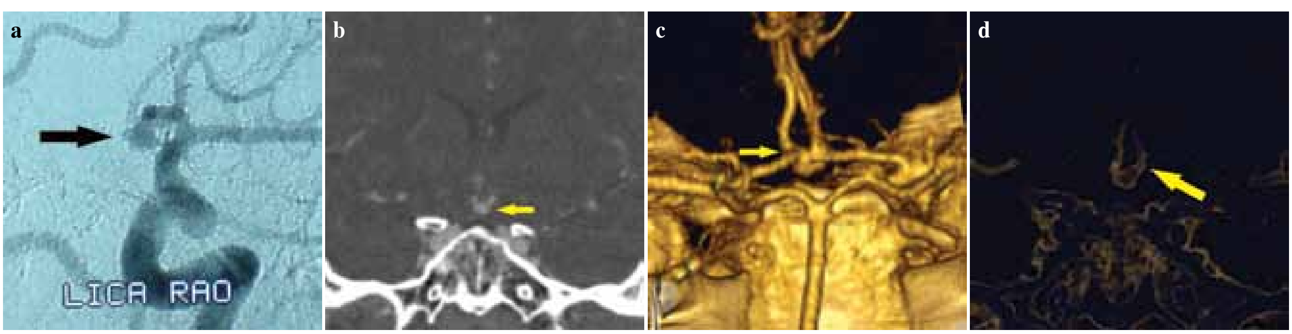

FIGURE 1. Aneurysm of the anterior communicating artery (ACoA) and its neck in a 27-year old male. (a) Selective intra-arterial digital subtraction angiography (DSA) of left internal carotid artery, detection of the aneurysm and its neck; (b) Computed tomographic angiography (CTA) coronal Multi-Planar Reformation (MPR) image of the aneurysm; (c) 3D-CTA, detects the 5-mm saccular aneurysm of the ACoA; (d) Coronal image of the aneurysm and its neck by the hollow vessel technique.

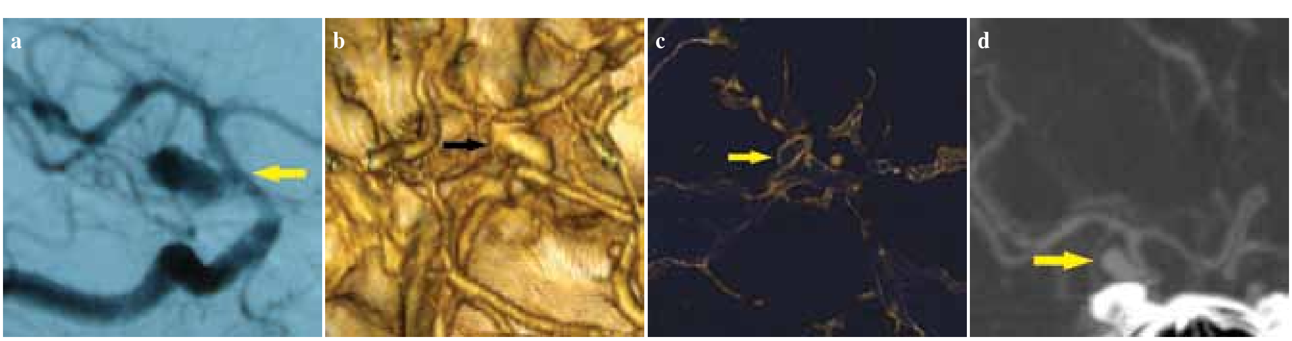

FIGURE 2. Right internal carotid artery (RICA) aneurysm and its neck in a 48-year-old female. (a) Selective intra-arterial digital subtraction angiography (DSA) of the right internal carotid artery (RICA), detection of the aneurysm and its neck; (b) 3-Dimentional Computed Tomographic Angiography (3D-CTA) depicts the 1.2cm supraclinoidsaccular aneurysm of RICA and its neck; (c) Axial image of the aneurysm becomes as in the previous one; (d) CTA, coronal Maximum Intensity Projections (MIP) of the aneurysm.

TABLE. Characteristics of aneurysms

Location	No. cases DSA	No. cases CTA
Anterior communicating artery	19	19
Posterior communicating artery	0	0
Middle cerebral artery	12	11
Anterior cerebral artery	2	2
Posterior cerebral artery	2	2
Basilar artery	2	2
Internal carotid artery	10	10
Size		
<3 mm	2	1
3-5mm	7	7
>5mm	38	38

multiple aneurysms, 5 of them had 2 aneurysms (3 aneurysms in the right MCA and 2 in the left MCA, 2 in the right ICA and 1 in the left ICA, 1 in the BA and 1 in the ACoA), while 1 patient had 3 aneurysms in the right ACA, in the ACoA and in the right ICA (Fig. 3).

According to DSA measurements, 2 of the aneurysms were ≤3mm, 7 of them 3-5mm and 38 aneurysms >5mm. The smallest aneurysm recognized by DSA was 2mm and the largest was 38mm (mean size 10.6mm). Vasospasm was detected in 21 patients by using DSA images. Using the same method we did not recognize any aneurysm with luminal thrombi and/or calcifications.

Correct diagnosis was made by using three-dimensional CTA in 46 out of overall 47 aneurysms which were detected by DSA. In a patient with two aneurysms CTA missed a 2mm aneurysm which was located in the left middle cerebral artery. However, retrospectively the aneurysm was depicted in the 2D and 3D CTA, but was overlooked by the two radiologists because of the generalized vasospasm, the very poor image quality and the acute status of the patient (Fig. 4).

Overall the sensitivity of CTA for the detection of intracranial aneurysms was 97.9% (CI 0.83-1), specificity 100% (CI 0.50-0.99), the positive diagnostic likelihood ratio 0 and the negative diagnostic likelihood ratio 0.02. The confidence intervals (CI) were 95%. In our study group we had only 2 aneurysms smaller than 3mm, therefore we could not reach any conclusions about sensitivity and specificity in this special group of aneurysms.

Based on CTA measurements, one of the aneurysms was ≤3mm, 7 of them were 3-5mm and 38 of them >5mm. The smallest of the aneurysms was 2mm and the largest was 38mm

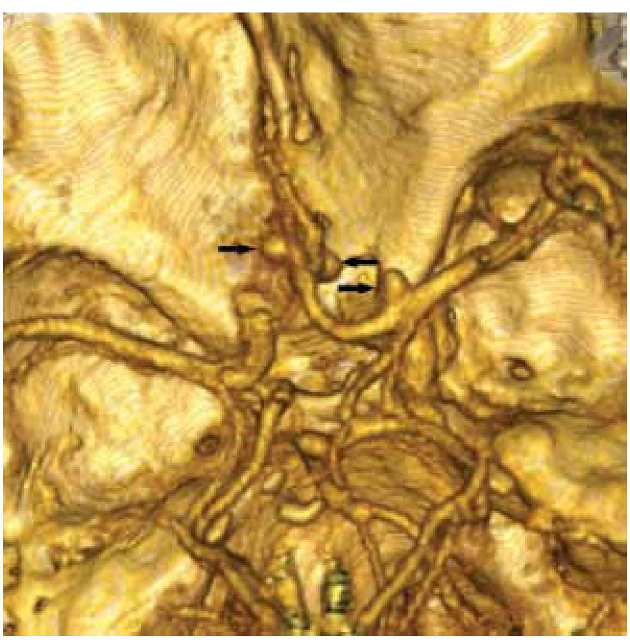

FIGURE 3. 3-Dimentional Computed Tomographic Angiography in the circle of Willis in a 44 year-old male. Three aneurysms were depicted, one in the right anterior cerebral artery, one in the anterior communicating artery and one in the right internal carotid artery.

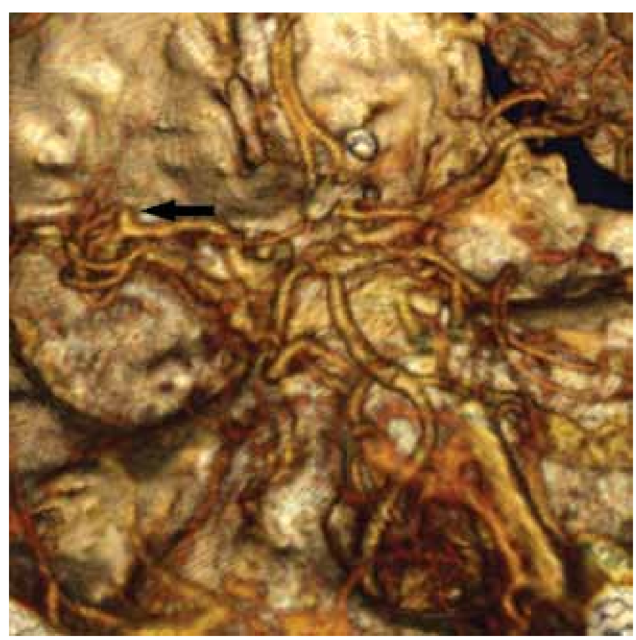

FIGURE 4. 3-Dimentional Computed Tomographic Angiography at 50 days follow-up in a 46-year-old woman with aneurysm's surgical clipping in anterior communicating artery. The aneurysm before the left middle cerebral artery bifurcation is the aneurysm which was missed.

(mean size 10.8mm). According to the neck width of the aneurysms the dimensions were between 1-8mm (mean size 3.3mm).

The post processing ability of CTA improved the morphological study and the determining of the aneurysms' orientation, 77.8% had an upward orientation and only 22.2% had a downward orientation. Only 6 aneurysms had luminal thrombi with calcifications (12.8%). There were vascular variances in up to 29.8% in our patient group. We also recognized vascular vasospasm in 17 patients. All these anatomical features were important for the therapeutic decision.[15]

Surgical or endovascular correlation was performed when it was possible. The aneurysms were treated in 23 patients either by endovascular coiling (65.2%) or by surgical clipping (34.8%). In those patients there were no new findings either with CTA or DSA. Only 3 patients with multiple aneurysms were treated, one of them had three aneurysms and the other two had twoaneyrysms. In the first patient two of the aneurysms were treated by endovascular coiling (in right ACA and in ACoA). In the other two patients surgical ligation was performed in only one of their two aneurysms (right MCA, left MCA).

From the other 17 patients of our study group, 9 died and the other 8 were treated elsewhere without any update.

Only 3 patients from those with negative CTA and DSA complied with the follow up instructions. The CTAs performed 20-30 days post SAH were negative. We did not establish any contact with the other 5 patients.

DISCUSSION

In our days invasive and non-invasive diagnostic angiographic techniques have been used for the early diagnosis of ruptured intracranial aneurysms in patients with SAH. In some centers CTA has almost completely replaced DSA in patients with SAH.[16] CTA is a modality with the ability to detect bone landmarks and the adjacent vascular structures to the aneurysm which is important for the treatment decision. Also it has a lower radiation exposure and is cheaper than DSA.[17]

Many earlier reports in the literature compared single-detector row CTA to selective cerebral angiography. Serugaet al[18] and Petersen et al[19] confirmed that the sensitivity of CTA ranges between 67% and 100% and specificity between 92% and 100%. Actually, the median sensitivity of CTA for depicting cerebral aneurysm has been reported to be around 90%.[20] White et al found that the sensitivity of CTA for aneurysms ≤3mm was about 61% and for larger aneurysms the detection rate increases to 96%.[21] By contrast, Villablanca et alreported a CTA sensitivity of 98-100% compared to 95% of DSA for aneurysms smaller than 4mm.[22]

More recent reports using 16-detector row CTA showed very good sensitivity and specificity too. Taschner et al showed CTA to have a sensitivity of 100% and specificity of 83% as compared with DSA.[23] Nijjar et al demonstrated a detection rate for CTA for depicting ruptured aneurysms up to 99.4% as compared with the results of surgical clipping.[24] El Khaldi et al calculated an overall sensitivity of 98.8% and specificity of 100% with a positive predictive value of 100%, negative predictive value of 95.2% and diagnostic accuracy of 99%.[25] However, for aneurysms smaller than 3mm Tripper et al[26] found a CTA sensitivity of 91.7% and Yoon et al reported sensitivity up to 77.8%.[10]

Our results with sensitivity up to 97.9% and specificity of 100% show a high diagnostic value of CTA in depicting ruptured intracranial aneurysms as have many recent reports in the literature. DSA successfully identified all 47 aneurysms and CTA missed only a small (2mm) aneurysm which was located in the left middle cerebral artery. Our results are in agreement with other reports in the literature.

Retrospectively the missed aneurysm was present as a perceptual error on the 2D and 3D CTA. Westerlaan et al believes that the possibility of missing a ruptured aneurysm in CTA is less than 2% and reported the effect of double reading with false negative rate smaller than 1%.[17] Peterson et al presented the importance of the observer's diagnostic experience with an increase in sensitivity a year later from 88% to 94%.[19]

Actually, CTA has a relatively high false negative rate to distinguish small aneurysms from bony structures near the skull base.[17] Retrospectively, the aneurysm which was misdiagnosed was apparent. In our case it was overlooked for other reasons as we have already mentioned. Actually, the aneurysms which were detected in the cavernous and supraclinoid area were not small. Their sizes ranged between 1 and 3.8cm and we did not have any difficulty in discerning them from the bones.

There are reports about CTA's difficulty to distinguish vascular infundibula of the posterior communicating or anterior choroidal artery from an aneurysm.[27] However, on our database there was not any respective experience of aneurysm's confusion with infundibulum on CTA or DSA. It is reported that the use of 64-row MDCTA with isotropic voxel resolutions of up to 0.4mm will improve the acquisition and post processing techniques with better results in detection of aneurysms especially in the posterior fossa.[17]

In the literature and in our study VRT and SSD method were helpful for anatomic and vascular details.[28] The anatomic information with 16 detector row CTA was satisfactory. All the normal vascular variances such as aplasia, hypoplasia or duplication of a vessel's segment were absolutely demonstrated. There were 8 patients with vascular aplasia, 2 with hypoplasia and 2 with duplication of arterial segments.

The anatomical features of the aneurysms, especially the location, size, neck width and dome/neck ratio indicate the choice of treatment.[4] In our study the morphologic characteristics of the aneurysms and the clinical condition of the patients were responsible for the final decision. Fifteen patients were treated by embolization with coils and 8 by surgical clipping.

Thrombus and calcifications are much more visible with CTA rather than DSA because this modality depicts the vessel's lumen, with better resolution of the wall and of the surrounding anatomy.[2] We detected 6 aneurysms with luminal thrombi and calcifications on CTA while DSA failed to detect such aneurysms.

Blood's density in the acute phase is a predictable factor for vasospasm.[29] Actually, clinical vasospasm corresponded to notable (>50%) vessel's constriction.[30] In our study DSA successfully recognized vasospasm in 21 patients and CTA in 17 patients. The DSA of the smaller vessels in distal locations allows for better depiction to a higher spatial resolution than CTA.[31]

Westerlaan et al in a recent systematic review and meta-analysis showed that CTA could be used as a primary examination tool for the imaging and treatment process for patients with acute onset of SAH.[17] They consider that for cost effectiveness issues DSA can be avoided if CTA is positive for intracranial aneurysms or is negative after radiologist's double reading. However, MacKinnon et al calculated a negative predictive value up to 93.2% and believed that the CTA for patients with acute SAH remains incomplete.[32] They suggest for confirmation the use of DSA in these patients, with an exception for patients with perimesencephalic syndrome. Agid et al reported that a negative CTA is enough when there is no evidence of blood on CT or in case of perimesencephalic pattern of SAH.[11]

Our study has some limitations. Our patient sample size was smaller compared to some other studies but the use of the DLR calculation instead of the predictive value, which is not dependent upon the prevalence of disease, improved our statistical analysis. Another limitation is the fact that CTA is compared to DSA as the gold standard method without comparison to surgical/endovascular or autopsy findings for all the patients because this was not included in our study. In the literature negative values of DSA in patients with SAH have been reported up to 10-20% while in 30% of them aneurysms were detected by repeat angiography.[33,34] The use of a 16-detector row CTA was a limitation in our study compared to more sophisticated detector row CTAs, but on the other hand our study proves that multi-detector CTA is an accurate diagnostic method for the detection of ruptured cerebral aneurysms even when lower sufficiency imaging equipment is used. Finally, in this study we review 3D images with 16-detector row CTA which has many advantages compared to 2D images obtained with DSA.

CONCLUSION

Based on the findings in our study cohort, 16-MDCTA is an accurate diagnostic method for the detection of ruptured cerebral aneurysms in patients with SAH. It is fast and simple to perform and is a non-invasive radiological technique without major complications. It can be used safely as an alternative to DSA for intracranial aneurysm detection even in secondary-county hospitals where more sophisticated and technologically improved imaging tools are not available. The only aneurysm that we missed was a small (2mm) aneurysm which was visible retrospectively. We believe that the combination of radiology's increasing experience and the availability of more advanced workstations will improve the sensitivity and specificity even for small (<3mm) aneurysm detection.

CORRESPONDING AUTHOR STATEMENT

The present study was supported solely by institutional and/or departmental sources and the publication was approved by all authors. All the authors have participated sufficiently in conducting the study and writing the article and take public responsibility for its content. The article is original and has not been previously published. The authors have no conflict of interest including financial or personal relationships.

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