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Performance of Contrast Enhanced Magnetic Resonance Angiography and CTA in the assessment of intracranial aneurysm coilability in patients with a subarachnoid haemorrhage

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Willem van Zwam, Paul Hofman, Alfons Kessels, Thoen Oei, Roel Heijboer, Jan Wilmink

Abstract

INTRODUCTION: This study aims to determine whether contrast enhanced magnetic resonance angiography (CEMRA) is preferable to computed tomographic angiography (CTA) as primary diagnostic tool in patients presenting with subarachnoid haemmorhage (SAH). When an intracranial aneurysm is the source of SAH it is of primordial importance to exclude it from circulation as soon as possible, preferably using endovascular coiling. The preferred diagnostic tool, therefore, must be able to quickly and accurately predict coilability of the aneurysm. In this study we evaluated both CEMRA and CTA in this aspect.

METHODS: Two experienced neuroradiologists evaluated CEMRA and CTA images of 75 consecutive patients with SAH. Accuracy in predicting coilability of aneurysms of both modalities was evaluated using digital subtraction angiography (DSA) as standard of reference.

RESULTS: 65 aneurysms were detected in 57 patients. No significant difference was found between the 2 modalities with respect to accuracy in assessing the feasibility of endovascular treatment: sensitivity and specificity for both were rather low (52.8-72.2 and 80.9-89.4 respectively), and Kappa was only 0.49 for both.

CONCLUSION: The diagnostic performance of CEMRA does not significantly differ to that of CTA in the work-up of patients presenting with SAH; additionally, both modalities are found to have a rather low accuracy in predicting coilability of intracranial aneurysms.

Keywords: magnetic resonance angiography, intracranial aneurysm, subarachnoid haemorrhage, computed tomography, angiography

Abbreviations

D2B	door to balloon
INSTOR	Interventional Stroke Therapy Outcomes Registry
MI	myocardial infarction
mRS	modified Rankin Scale
NIHSS	National Institute of Health Stroke Scale
SICH	symptomatic intracerebral hemorrhage

Willem van Zwam, MD MSc (Corresponding Author) — Department of Radiology, Maastricht University Medical Centre, PO Box 5800, 6202 AZ Maatricht, The Netherlands *Tel:* +31 433876910 *Fax:* +31 433876909 *Email:* w.van.zwam@mumc.nl

Paul Hofman, MD PhD — Department of Radiology, Maastricht University Medical Centre, Maastricht, The Netherlands

Alfons Kessels, MD PhD — Department of Clinical Epidemiology and Medical Technical Assessment, Maastricht University Medical Centre, Maastricht, The Netherlands

Thoen Oei, MD — Department of Radiology, Maastricht University Medical Centre, Maastricht, The Netherlands

Roel Heijboer, MD — Department of Radiology, Atrium Medical Centre, Heerlen, The Netherlands

Jan Wilmink, MD PhD Prof — Department of Radiology, Maastricht University Medical Centre, Maastricht, The Netherlands

SITS-MOST	Safe Implementation of Thrombolysis in Stroke Monitoring Study
TIMI	thrombolysis in myocardial infarction
TICI	thrombolysis in cerebral infarction
tPA	tissue plasminogen activator

Introduction

When subarachnoid haemorrhage (SAH) is diagnosed, computed tomographic angiography (CTA) is the modality generally used to ascertain whether a cerebral aneurysm is present [1]. Subsequently, CTA can also be used to assess the feasibility of endovascular treatment of the aneurysm [2-7].

There are some general advantages to magnetic resonance angiography (MRA) over CTA: potentially harmful ionising radiation is absent, and no iodinated contrast agent is administered. However, flow dependent MRA sequences like time of flight MRA can suffer from signal loss, due to in-plane saturation or turbulent flow inside an aneurysm [8]. In this context, therefore, contrast enhanced MRA (CEMRA) may be a preferable diagnostic tool. Besides a very small risk of nephrogenic systemic sclerosis or adverse reactions on Gadolinium-based contrast agents, the major disadvantage of MRA is that it requires transfer of the patient to the MRI room, whereas additional CTA requires little extra effort since CT is the standard used to confirm the presence of SAH. Given these factors, CEMRA should only be recommended if it performs significantly better than CTA.

In a previous publication, we demonstrated that CEMRA performance was equal to that of CTA in detecting aneurysms in patients with SAH [9], which was in concordance with previous publications on this topic [10-12]. In this study, we compared the accuracy of CEMRA and CTA in predicting coilability of such aneurysms.

Materials and Methods

Study design

From 2004 to 2006, all adult patients with diagnosed non-traumatic SAH were eligible for inclusion in our study. All patients underwent standard CTA in order to detect the presence of intracranial aneurysms as the source of bleeding and, when such an aneurysm was found, to assess suitability for endovascular treatment.

Patients meeting study inclusion criteria underwent an additional CEMRA study before endovascular or surgical treatment and within 48 h after CTA. We ensured, however, that the additional CEMRA study did not delay treatment. Informed consent was obtained from all patients or, for patients who were unable to give informed consent, from legally authorised representatives.

Actual aneurysm coilability found during the coiling procedure was used as the reference standard, and in situations where no coiling was performed, diagnostic DSA served as reference standard. Approval for this study was obtained from the Institutional Review Board of our hospital, as well as from the Centrale Commissie Mensgebonden Onderzoek (Central Committee Human-Related Research) (CCMO); the latter was required due to the possible inclusion of patients unable to give informed consent.

Patients

All consecutive adult patients having obtained a CT or lumbar puncture diagnosis of non-traumatic SAH were eligible for inclusion in this study. Exclusion criteria were: a contraindication for magnetic resonance imaging (MRI) or no further treatment requirement. Poor clinical condition was not an exclusion criterion, but where the treating physician considered chances of survival to be nil, no further diagnostic or treatment procedures were undertaken and the patient was excluded from the study.

Techniques

CTA:

CTA was performed on a two-slice (Elscint Dual, Elscint, Haifa, Israel) or four-slice multidetector-row spiral CT scanner (Toshiba Aquilion, Toshiba, Tokyo, Japan). Scan parameters were: 120 kVp, 250 mAs, collimation width 1.3 mm, pitch 0.7; FOV 250 mm, matrix 340x340 for the two-slice scanner; and 120 kV, 200 mAs, collimation width 0.9 mm, pitch 0.67; FOV 230 mm, matrix 512x512 for the four-slice scanner. For both scanners a 0.5 mm slice reconstruction was used. Contrast material used was iobitridol 350 mg/ml (Xenetix®, Guerbet, Villepinte, France), administered IV at 4 ml/s, total volume 125 ml and flushed with 40 ml NaCl 0.9 % at 4 ml/s. For the Elscint scanner we injected an extra test-bolus of 20 ml contrast material in order to determine the optimal interval between start of contrast injection and start of the scan. For the Toshiba scanner we made a detection slice through the internal carotid arteries; scans were started upon arrival of contrast in this slice. In both scanners scan direction was caudal to cranial.

In most cases we used a semi-automatic bone subtraction method, matched mask bone elimination (MMBE): a low dose-mask is acquired from the bony skull, after which the bone-containing voxels are extracted from post-contrast images, using a computer algorithm which compensates for any movements of the patient between scans [13, 14]. Where a patient was too restless to undergo a mask CT scan or where the contrast scan could not be matched with the mask, bony structures were subtracted from the contrast scan using manual segmentation.

MRA:

MRA was performed on a 1.5 Tesla Philips scanner using a dedicated head coil (Intera, Philips, Best, The Netherlands). The scan protocol included an ultra-short first-pass CEMRA with concentric k-space filling. The scan parameters were: parallel imaging (SENSE, factor 2), TR 5.4 / TE 1.68 ms, flip angle 35 deg, FOV 256 mm (Rectangular FOV 65 %), matrix 512, slice thickness 0.4 mm, coronal orientation (parallel to basilar artery), one stack. Contrast material used was gadopentetate dimeglumine 35 ml (Magnevist®, Bayer Schering Pharma, Leverkusen, Germany), administered IV at 3 ml/s (2 ml for a timing sequence and 33 ml for the CE-MRA sequence) and flushed with 25 ml NaCl 0. 9 % at 3 ml/s.

DSA:

All patients underwent conventional catheter DSA (Integris, Philips Medical Systems, Best, The Netherlands). All 4 brain feeding arteries were catheterised and imaged, except for cases in which patient unrest allowed only the vessel containing the suspected aneurysm to be catheterised. A 4 or 5F catheter system was used in diagnostic DSA; a 6F catheter system was used in cases of anticipated immediate treatment. Automatic contrast material injections were performed by power injector (Medrad Inc., Warrendale, PA, USA): 9 ml iobitridol 350 mg/ml (Xenetix®, Guerbet, Villepinte, France) at 5 ml/s for the carotid arteries, and 8 ml at 4 ml/s for the vertebral arteries. Projections obtained were antero-posterior, lateral and oblique for internal carotid arteries, and antero-posterior and lateral for vertebral arteries. Where necessary in order to better visualise an aneurysm, its neck and surrounding arteries, additional angiographic projections were obtained of vessels harboring an aneurysm.

Image interpretation and statistical analysis

CTA and MRA data were sent to a post-processing workstation (Vitrea, Vital Images, Minnetonka, Minnesota, USA) and interactively evaluated. Two experienced neuroradiologists each evaluated both modalities in random order. Scoring criteria used were: quality of images, coilability of any aneurysm and diagnostic confidence. Coilability was defined as "coiling feasible without adjunctive devices". No pre-defined anatomical criteria like dome-to-neck ratio were requested and the decision was left to the discretion of the observer. Diagnostic confidence was rated on a three point scale.

The performance of each modality in the prediction of coilability of an aneurysm was evaluated using calculations of sensitivity, specificity and ROC curves. In addition, Cohen's Kappa for inter observer agreement was calculated. In ROC curve calculations, confidence scoring was transferred to a negative value if the aneurysm was considered non-coilable and the resulting values were used as cut-off points.

Results

Of 189 patients eligible for inclusion, 114 (60.3 %) could not be included in the study for reasons outlined in Table 1. Seventy-five patients were included: 50 with 1 aneurysm, 6 with 2 aneurysms and 1 with 3 aneurysms. A total of 65 aneurysms were found. In 18 (24 %) patients no aneurysm was found. Of the aneurysms found in our study population, 50.8 % (33/65) were smaller than 5 mm, and 18.5 % (12/65) were smaller than 3 mm.

The sensitivity and specificity of CTA and CEMRA for the assessment of coilability of aneurysms are given in Table 2a. All 75 patients were included in these calculations; the 18 patients who did not have aneurysms were classified as "coiling not feasible". There was no significant difference between the sensitivity and specificity of CTA and CEMRA as assessed with McNemar's test statistics.

Cohen's Kappa for inter-observer agreement on the assessment of coilability of aneurysms was 0.49 for both CEMRA and CTA.

ROC curves for the prediction of aneurysm coilability are shown in Figure 1. The areas under the curve are 0.73 (0.62 – 0.83) and 0.78 (0.69 - 0.88) for CTA and 0.71 (0.60 – 0.81) and 0.77 (0.67 - 0.86) for CEMRA. These did not differ significantly between CTA and CEMRA ($p=0.75$ for observer 1 and $p=0.83$ for observer 2).

Sensitivity and specificity for prediction of coilability of aneurysms, calculated only for those patients for whom one or more aneurysms were detected, are given in Table 2b; Cohen's Kappa, based on these cases only, decreased to 0.38 for CTA and to 0.46 for CEMRA.

Discussion

The added value of CTA in the work-up of patients presenting with SAH has been subject to debate [15-17]. When CTA does not show an aneurysm, DSA will be carried out, and when CTA does detect an aneurysm, DSA is often required to decide whether or not endovascular treatment is possible. Therefore, only a CTA capable of providing sufficient information to both detect an aneurysm and allow for a reliable decision to be made about treatment, could ever belong in the diagnostic toolkit for SAH.

Several papers describe the capacity of CTA to select the appropriate treatment for intracranial aneurysms [2-7, 18-20]. Most authors conclude that CTA is able to correctly guide treatment planning in the majority of cases, thus limiting the need for additional DSA [2, 4, 18]. Few studies have described the use of MRA in assessing feasibility of endovascular treatment [10, 11, 21, 22], and none make a direct comparison with CTA. The conclusions of these studies vary from “MRA appears to be an effective treatment planning tool for most patients with SAH” [21], to “MRA cannot replace DSA in treatment planning” [11].

In this study we show that CEMRA and CTA perform equally well in the determination of coilability of intracranial aneurysms in patients with a SAH. However, sensitivities for both modalities are rather low, between 52 and 74 %, and interobserver agreement is only moderate (Kappa 0.49).

One reason for the low interobserver agreements is that the decision of whether an aneurysm can be treated by endovascular means is largely a subjective one. Even though some anatomical characteristics of an aneurysm, such as large neck-to-dome ratio and vessels emerging from the base of the aneurysm, are relative contra-indications for endovascular treatment, the decision on how to treat the aneurysm largely depends on insight and experience of the observer (Figure 2). To investigate this aspect we asked two experienced neurointerventionists from two different hospitals to give their opinion, independent of each other, on the feasibility of endovascular treatment based on DSA findings of our patients with an aneurysm; Kappa was only 0.41. Of the 65 evaluated aneurysms, the first observer considered 46 aneurysms were suitable for endovascular coiling, whereas the second observer considered only 33 aneurysms suitable (see Table 3). This clearly illustrates one limitation of the DSA as standard of reference as it is largely dependent on subjective criteria.

All 75 patients were included in our calculations because the observer evaluated them all for aneurysm presence, as well as for coilability if an aneurysm was found. There was no false negative score for coilability in this study due to a potentially coilable aneurysm that was not detected, nor was there a false positive for the presence of falsely detected aneurysm which was subsequently considered coilable.

We have previously shown that CEMRA and CTA perform equally for detecting intracranial aneurysms [9]. In the present study we show that CEMRA is not preferable to CTA in assessing coilability of the aneurysms found. We found that 36 of 65 aneurysms appeared to be suitable for endovascular treatment based on DSA. In 2 of these patients, an endovascular procedure was initiated but coiling proved to be impossible. In these cases, the procedure was aborted and patients were referred for surgery. In our analysis we included these aneurysms in the not suitable for endovascular treatment group, reflecting the findings during the endovascular procedure. Thus, in our study, 34 of the 65 aneurysms (52.3 %) were treated by coiling, which is fewer than average in our overall population of patients with an aneurysmal SAH [23].

Even allowing for the above difficulties in assessing true coilability of an intracranial aneurysm, it appears that the accuracy of CEMRA is simply not good enough to advise its use in the work-up of patients with SAH. CTA should remain the modality of choice, especially in view of the recent evolution in CTA technique, and DSA remains essential whenever coilability remains uncertain based on CTA images..

Conclusion

The performance of CTA and CEMRA in assessing the suitability of aneurysms for endovascular coiling is similar. Therefore CTA remains the modality of choice in patients presenting with SAH. In addition, we showed that the ultimate decision on whether an aneurysm can be coiled is very subjective. The information provided by non-invasive imaging techniques has an important function in the therapeutic decision process in patients presenting with SAH, but to date additional diagnostic DSA remains necessary in a considerable number of cases. Only when the diagnostic performance of techniques such as CTA and CEMRA improve, will the need for additional DSA decrease.

Conflict of interest

We declare that we have no conflict of interest.

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Figures

Figure 1 - ROC curve for the feasibility of endovascular treatment by CTA and CEMRA by both observers.

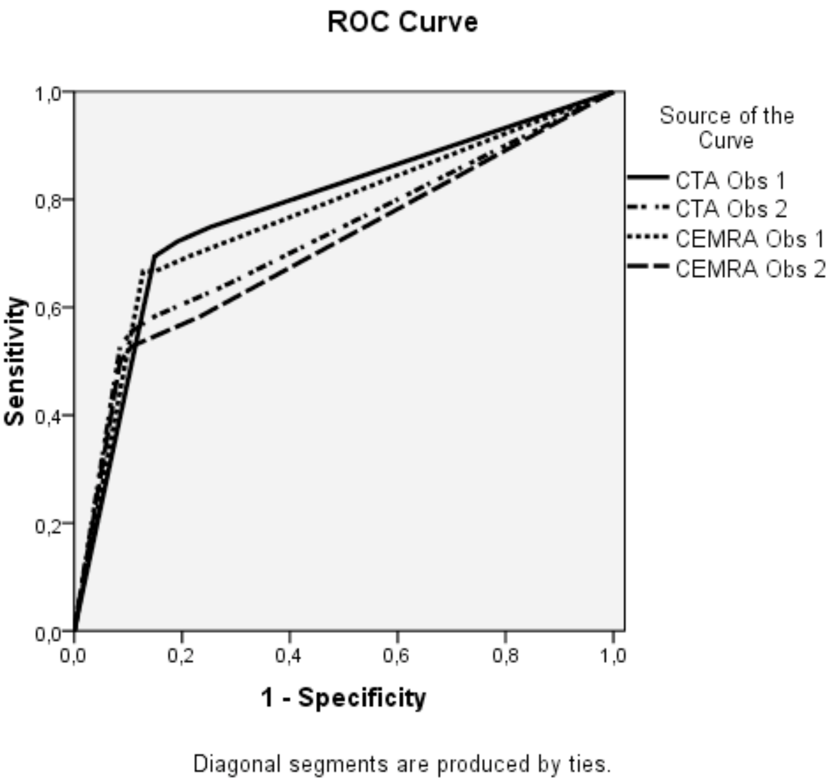
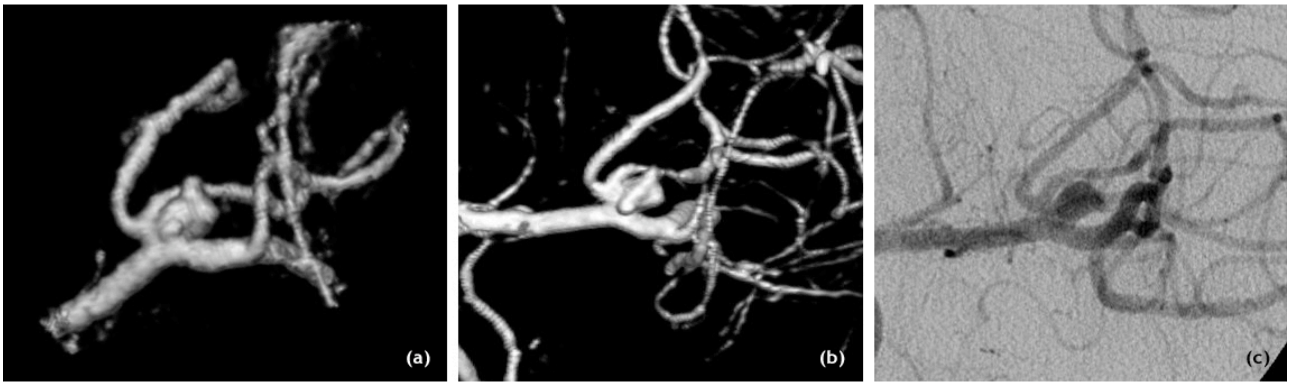


Figure 2 – Left middle cerebral artery aneurysm.



(a) 3D reconstructed image from CTA.
(b) 3D reconstructed image from CEMRA.
(c) DSA image. One observer considered this aneurysm coilable on both CTA and CEMRA images while the other observer considered the aneurysm as not coilable on both modalities. The aneurysm was considered coilable on the DSA image and subsequently successfully coiled.

Tables

Table 1 - Reason for exclusion

Reason for exclusion	**N**
- Not enough time between CTA and treatment to perform MRA	57
- Declined additional MRA	22
- Condition too poor to plan further treatment	11
- Contra-indication for MRI	10
- Patient distress, MRA not possible	6
- Died before MRA	4
- No informed consent before treatment (no MRA made)	2
- Died before DSA and treatment, after MRA	1
- Transferred to other hospital for treatment	1
Total excluded	**114**

Table 2 - Sensitivity and specificity tables

Table 2a		**CTA**	**CEMRA**
Sensitivity	Obs 1	55.6 (38.1 - 72.1)	52.8 (35.5 - 69.1)
	Obs 2	72.2 (54.8 - 85.8)	66.7 (49.0 - 81.4)
Specificity	Obs 1	89.4 (76.9 - 96.5)	89.4 (76.9 - 96.5)
	Obs 2	80.9 (66.7 - 90.9)	85.1 (71.7 - 93.8)

Table 2b		**CTA**	**CEMRA**
Sensitivity	Obs 1	62.5	52.8
	Obs 2	81.3	76.9
Specificity	Obs 1	80.8	80.8
	Obs 2	70.4	68.6

(a) Sensitivity and specificity (95% CI) of CTA and CEMRA for assessing suitability for endovascular treatment (coilability) of an aneurysm.

(b) Sensitivity and specificity of CTA and CEMRA for assessing the coilability of an aneurysm including only those patients in whom an aneurysm was found (as scored by the observer).

Table 3 - Ratings of two independent, experienced neurointerventionists on the suitability for endovascular treatment (coilability) of intracerebral aneurysms based on DSA.

		Coiling feasible Obs 2		
		no	*yes*	**Total**
Coiling feasible Obs 1	*no*	16	3	**19**
	yes	16	30	**46**
	Total	**32**	**33**	**65**