Three Dimensional CT Angiography Versus Digital Subtraction Angiography in the Detection of Intracranial Aneurysms in Subarachnoid Hemorrhage.

Charles J. Prestigiacomo MD

Aria Sabit

Wenzhuan He
Lehigh Valley Health Network, wenzhuan.he@lvhn.org

Pinakin Jethwa

Chirag D. Gandhi MD

See next page for additional authors

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Authors

Charles J. Prestigiacomo MD, Aria Sabit, Wenzhuan He, Pinakin Jethwa, Chirag D. Gandhi MD, and Jonathan Russin

Three dimensional CT angiography versus digital subtraction angiography in the detection of intracranial aneurysms in subarachnoid hemorrhage

Charles J Prestigiacomo,[1,2,3] Aria Sabit,[4] Wenzhuan He,[1] Pinakin Jethwa,[1] Chirag Gandhi,[1,2] Jonathan Russin[5]

[1]Department of Neurological Surgery, UMDNJ, Newark, New Jersey, USA
[2]Department of Radiology, UMDNJ, Newark, New Jersey, USA
[3]Department of Neurology, UMDNJ, Newark, New Jersey, USA
[4]Ventura Neurosurgical Associates, Ventura, California, USA
[5]Department of Neurological Surgery, Los Angeles, California, USA

Correspondence to
Dr C J Prestigiacomo, Department of Neurological Surgery, Radiology and Neurology, University of Medicine and Dentistry of New Jersey, 90 Bergen Street, Suite 8100, Newark, NJ 07101, USA; c.prestigiacomo@umdnj.edu

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ABSTRACT

Introduction Ruptured intracranial aneurysms are responsible for over 90% of cases of spontaneous subarachnoid hemorrhage (SAH). Conventional digital subtraction angiography (DSA) remains the gold standard for diagnosing the source of SAH. A prospective study is presented wherein SAH patients underwent three dimensional CT angiography (CTA) prior to DSA in order to assess the specificity and sensitivity of this non-invasive modality to detect aneurysms.

Methods 179 consecutive patients with spontaneous SAH presented over 36 months, as identified by screening CT and CTA. Patients with negative CTA findings underwent DSA within 24 h of presentation. All patients who were determined to have angiographically negative SAH underwent follow-up DSA 2 weeks later.

Results Of the 179 patients screened by CTA, 13 (7%) were negative for aneurysms or other vascular lesions (arteriovenous malformation or dural fistula) on CTA and underwent DSA. No new lesions were identified on six vessel angiography, resulting in a 0% false negative rate (sensitivity 100%, predictive value 100%). MRI to rule out thrombosed aneurysms and repeat angiography at the 2 week follow-up were negative.

Conclusions Sensitivity and specificity were higher than previously reported, suggesting that CTA may be used as an initial screening tool in lieu of DSA. Further studies are necessary to determine if CTA can supplant DSA in ruling out all forms of vascular disease in idiopathic SAH.

INTRODUCTION

Intracranial aneurysm rupture is the etiology for at least 85% of all patients sustaining spontaneous subarachnoid hemorrhage (SAH).[1] Since its introduction in 1927, catheter based digital subtraction angiography (DSA) has been the gold standard in the detection of intracranial aneurysms. However, DSA is an invasive, time consuming and relatively expensive procedure with the limitations of contrast medium load and radiation dose. It has been associated with a 0.3–0.8% rate of serious non-neurological complications, a 0.5–2.3% rate of transient neurological complications and a 0.1–0.5% rate of permanent neurological complications.[2 3] In the setting of aneurysmal SAH, DSA has also been suggested to have a 2.6% rate of re-hemorrhage if DSA is performed within 6 h after the initial ictus.[4 5] Over the past decades, less invasive imaging modalities, such as CT angiography (CTA) and MR angiography (MRA), have been increasingly evaluated as a means of detecting ruptured intracranial aneurysms.

MRA has been an attractive alternative to conventional angiography due to its risk free, non-invasive nature. Added advantages of this technique are its ability to produce images in three dimensions and the ability to produce many projections after a single acquisition, and the technique forms a routine part of an MRI investigation for cerebral aneurysms.[6] However, a variety of artifacts by phase or magnitude variations in the MR signal afflict MRA and has limited its use, especially in preoperative planning of vascular malformations and aneurysms.[7]

Recently, the advent of CTA has been used in the diagnosis and preoperative planning for patients presenting with aneurysmal SAH.[8 9] It has been suggested that CTA has several advantages over MRA. These advantages include: CTA possesses greater resolution than MRA[10]; CTA is unique in its capacity to display the relationships of arteries and aneurysms to bone, which contributes greatly to preoperative planning for patients presenting with aneurysmal SAH[11 12]; CTA can be performed in seconds and can be performed immediately after the unenhanced CT has confirmed an SAH.[12 13] Indeed, with continued improvements in imaging, hardware and concomitant software enhancements, the sensitivity and specificity of CTA approaches that of DSA.[14] However, whether or not CTA can be used as the sole modality to provide sufficient diagnostic information to guide the management of non-traumatic SAH still needs further clinical evidence.[15–18] This study was conducted for this purpose.

METHODS

Institutional Review Board approval was acquired. A total of 179 consecutive patients who presented to University Hospital, Newark, New Jersey, USA, between October 2002 and October 2005 with a diagnosis of spontaneous SAH were included in the study. The diagnosis was made by CT evidence of subarachnoid blood or positive lumbar puncture in instances where CT imaging was negative for subarachnoid blood.

Once spontaneous SAH was confirmed, CTA was performed using a GE System 16 slice CT scanner with 150 ml Omnipaque pump injected at 4 ml/s with an 18 s acquisition delay, at 120 kV and 440 mA. Scans extended from the C1 vertebra to the vertex with a 0.625 mm slice thickness, at

0.625 mm intervals. Total scan time for this portion of the study was 15 s. Source images were transferred to a GE Advantage computer workstation where post-processing and evaluations were performed. Maximum intensity projections (MIP) and three dimensional reconstructions were performed by members of the neurosurgical team trained in the use of CTA technology (figure 1). All images, including source images, were independently reviewed by the senior member of the cerebrovascular team (CJP). Patients with an identified aneurysm on CTA were then evaluated for possible microsurgical clipping or coiling of the aneurysm.

Patients selected for endovascular treatment underwent a full, four vessel study to confirm the CTA findings, assess for any additional aneurysms and treat the ruptured aneurysm. Patients selected for microsurgical clipping were taken to the operating room for treatment, with intraoperative confirmation of the size and configuration of the aneurysm. Postoperative angiography was performed on all patients undergoing microsurgical clipping to assess for any residual aneurysms and to assess for the presence of any additional aneurysms. In order to minimize the risk of contrast induced nephrotoxicity, all patients were maintained at 1–1.5×maintenance intravenous hydration with normal saline. Patients with a serum creatinine of 1.0 or greater were treated with N-acetylcysteine for 48 h at a dose of 600 mg by mouth, twice daily. Patients with no evidence of aneurysm on CTA underwent six vessel DSA, supplemented with three dimensional rotational angiography (bilateral external carotid arteries, internal carotid arteries and vertebral arteries) to definitively rule out an intracranial aneurysm or other vascular anomaly. If creatinine was greater than 2.5, we would consider initiating sodium bicarbonate intravenously as an adjunct.

RESULTS

Of the 179 patients, 57 (31.9%) were men and 122 (68.1%) were women. Mean age of the patients was 52.9±13.7 years (range 14–85). Thirteen patients had a negative CTA and a negative DSA within 24 h of the initial CTA and negative results with repeat CTA and DSA during follow-up. One hundred and sixty-six patients had at least one intracranial aneurysm detected, with a total of 238 aneurysms detected on CTA. One hundred and twenty-five (77.1%) patients had a single aneurysm and 41 (22.9%) had multiple aneurysms, with a maximum number of eight aneurysms in a patient. One hundred and fourteen (68.7%) of the patients were women and 52 (31.3%) were men. All aneurysms were confirmed either by direct visualization at surgery or by DSA at the time of endovascular treatment. No neurologic or renal complications from CTA or DSA studies were noted.

All patients selected for microsurgical clipping were taken to the operating room for treatment based on information from CTA alone. The surgical findings, including the number of aneurysms, location and size were well correlated with CTA findings and no new information was found during operation.

The distribution of all aneurysms based on location (figure 2), size (table 1) and neck width (table 2) in this cohort was recorded. The smallest detected aneurysm on CTA was 1.4 mm although resolution of the distal vasculature on source images was in the submillimeter range. As can be seen, the majority of aneurysms detected in this series (212 (88.7%) aneurysms, both ruptured and unruptured) were under 10 mm in size with 45 (19%) aneurysms were less than 3 mm in size.

Importantly, DSA detected only one additional aneurysm along the distal posterior inferior cerebellar artery that was not detected prospectively on the CTA at the time of the patient's presentation. In other words, of the 239 aneurysms that were detected by DSA, 238 (99.6%) were initially detected by CTA at the time of the patient's initial presentation. Thus the sensitivity of CTA in detecting aneurysms was 99.6% and specificity was 100% compared with DSA. The predictive value of a positive CTA was 100% (ie, there were no false positive aneurysms found on CTA). Thirteen (7.3%) patients of the 179 patients who presented with SAH did not demonstrate an aneurysm on either CTA or DSA. The predictive value of a negative CTA in our series was 92.9% (per patient).

DISCUSSION

Over the past decade, increasing studies had been conducted to evaluate the effectiveness of CTA in detecting aneurysms. These

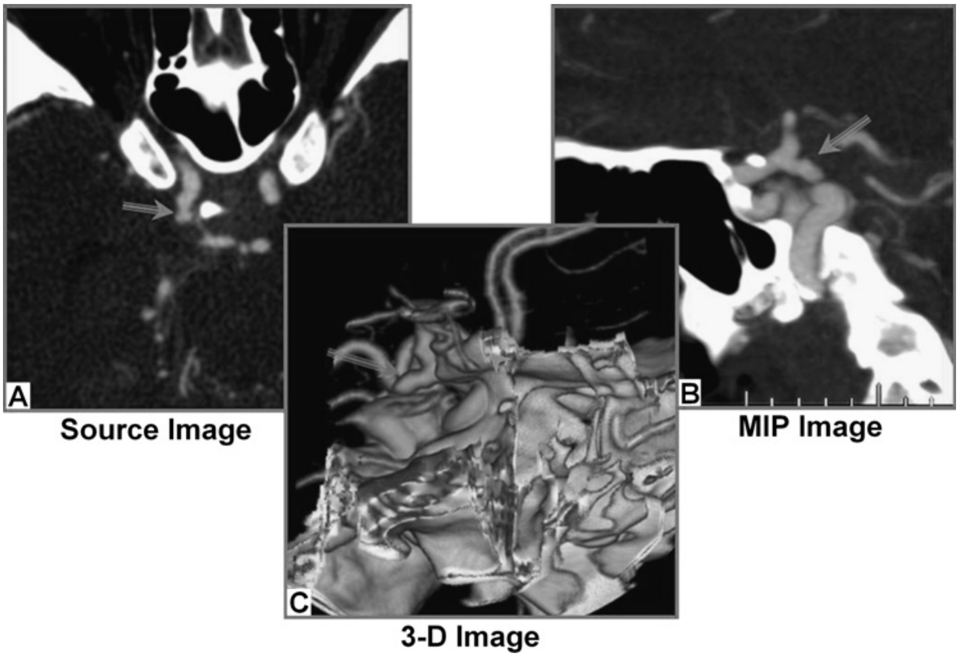

Figure 1 Protocol performed during the processing of the CT angiography images. (A) Source image: arrow points to the detected aneurysm. (B) Maximum intensity projection (MIP) image: arrow points to the detected aneurysm. (C) Three dimensional (3-D) image: arrow points to the detected aneurysm. Arrowhead demonstrates clinoid.

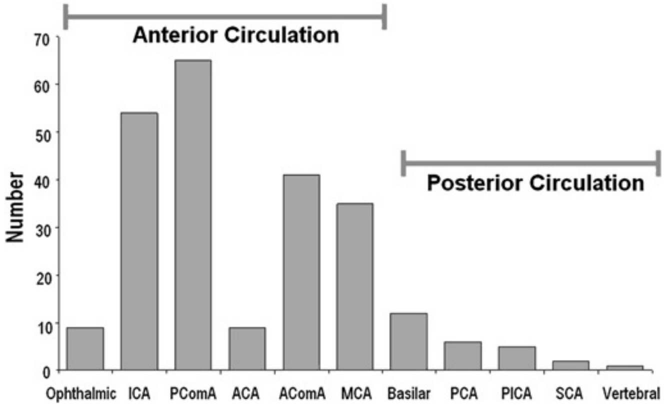

Figure 2 Bar graph stratifying the location of the aneurysm and its frequency in this study cohort. ACA, anterior cerebral artery; AComA, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; PComA, posterior communicating artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery.

studies reported variable sensitivity and specificity values ranging from 67% to 100% and 86% to 100%, respectively.[8 18–21] One study[19] compared CTA with DSA in detecting aneurysms in SAH patients and reported a sensitivity of 91% and specificity of 95% after 1 year's experience of using CTA. In this report, 13 out of 144 aneurysms were missed by CTA. However, 11 aneurysms were visible during post-angiographic CTA reconstructions. In another study, Jayaraman and colleagues[22] reported a sensitivity of 90% and specificity of 93% in one reader and 81% and 93% in another reader. All "missed" aneurysms by both readers were identified at retrospective reading. In our study, one of the 239 aneurysms that was detected by DSA was missed initially by CTA at the time of the patient's initial presentation. Retrospective review of the CTA source images clearly demonstrated this missed aneurysm, which had been inadvertently eliminated during the post-processing of the reconstructed three dimensional rotational imaging. Had the reconstruction incorporated the distal posterior inferior cerebellar artery, the aneurysm would have been recognized (as was noted on the subsequent reconstruction). All of these studies, including our study, suggest that CTA as a diagnostic imaging modality is highly sensitive in detecting aneurysms. But, interpreting CTA images is reader dependent. With more experience, CTA can be more sensitive. Pedersen *et al* demonstrated that there is a learning curve for CTA when they compared aneurysmal detection rates (94% vs 88%) in two consecutive years (1998 vs 1997). We believe, with more experience in interpreting CTA images, its sensitivity will be high enough to act as the sole image modality to provide sufficient diagnostic information to guide management of non-traumatic SAH. This was shown in a systematic review[23] which demonstrated that CTA studies published before 1995 had an accuracy per subject of 84% compared with an accuracy of 93% in CTA studies published after 1994.

Table 1 Size distribution of the aneurysms

Size (mm)	Frequency
1–2.9	45
3–4.9	81
5–6.9	47
7–9.9	39
10–14.9	19
15–20	6
>20	2
Total	239

Table 2 Maximum neck width of the aneurysms

Neck width (mm)	Frequency
1–2.4	39
2.5–3.9	81
4–4.9	53
5–7.4	48
7.5–10	11
>10	7
Total	239

Previous studies have suggested that CTA has limited sensitivity for aneurysms smaller than 3 mm compared with DSA.[24 25] White *et al*[25] reported a sensitivity of only 40% in aneurysms smaller than 3 mm with an overall sensitivity of 62%. Wintermark *et al*[24] reported a sensitivity of 50% in aneurysms less than 2 mm and a sensitivity of 95.8% in aneurysms greater than 2 mm. These results of early studies demonstrated relatively poor sensitivity of CTA in detecting aneurysms which were smaller than 3 mm. In our study, 88% of CTA detected aneurysms were less than 10 mm. Among these aneurysms, 19% aneurysms were less than 3 mm with the smallest aneurysm of 1.4 mm.

The high sensitivity and specificity of our study may be attributed to several factors. Technical advances in CTA, such as the 16 slice CT scanner and the more recent 64 slice scanners, have made the resolution of images obtained by this technique approximate the gold standard of DSA. With this technique, detection of aneurysmal size less than 3 mm has been dramatically improved. In addition to interval improvements in the software packages for the work station, a stringent protocol has been established in our institution defining the steps performed during the processing of the images. Initially, all source images are carefully evaluated slice by slice after appropriate windowing (approximating bone window parameters) has been performed. Any irregularities of the arterial tree detected during this phase of the evaluation are carefully studied on the next step. MIPs are then evaluated in three orthogonal planes, with slab thicknesses ranging from 1 to 4.5 mm. Once again, careful analysis of any irregularities is assessed. Once all major branches of the arterial tree are assessed, three dimensional reconstructions are reviewed for final analysis. Thus multiple examinations of the study by different post-processing techniques and by different members of the house staff are performed for each study. Furthermore, full review of the studies is also performed by the attending neuroendovascular specialist or cerebrovascular surgeon. These steps have assured that the entire cerebrovascular tree is carefully assessed from its most proximal to its most distal extent prior to making the final determination of whether an aneurysm is identified.

Another characteristic of our study is that all patients selected for microsurgical clipping were taken to the operating room for treatment based on information from CTA alone. The surgical findings, including the number of aneurysms, location and size, were well correlated with CTA findings and no new information was found during operation. Although patients who were selected for endovascular treatment and patients with no evidence of aneurysm on CTA underwent a full four vessel study or six vessel DSA to confirm the CTA findings, these DSA studies yielded only one previously undetected aneurysm in a patient who harbored multiple aneurysms. As noted, this additional aneurysm was visible on retrospective review of the CTA source images. Our result suggests that CTA can be used as the sole image modality to guide treatment in at least a subset of, if not all, patients with SAH. This result is consistent with previous studies.[26–28]

Furthermore, from figure 2 we can see the distribution of all aneurysms in the study. The 'ICA' category includes patients who had aneurysms identified in the paraclinoid and paracavernous region as well as along the course of the supraclinoid carotid artery but does not include aneurysms of the posterior communicating artery. Although difficult, as suggested by previous studies,[19 29 30] our study demonstrated that detecting aneurysms located near the skull base or near the bone and near the cavernous sinus is possible. One possible contributor to the detection of aneurysms in this difficult location is due to the acquisition time delay. Our protocol's acquisition delay enables excellent resolution between parabasal arteries and the cavernous sinus, the most difficult confounder in this region. Indeed, broad based, small ophthalmic aneurysms of this region require very careful scrutiny. Source images and MIP projections are able to distinguish these often subtle irregularities in our studies. The incorporation of bony anatomy in the three dimensional reconstructions also aids in the surgical planning of these lesions.

Although this study represents a prospective database, there are biases to the study which may affect the specificity analysis. Because of the nature of the study, suspicion of aneurysms in all patients is high and therefore the true negative rate may be difficult to assess. Based on this small subpopulation of patients, the false negative rate for CTA was 0%. Additionally, one would expect that this study would bias the investigators to 'over-call' an aneurysm on CTA, a false positive result. However, the false positive result was 0% in this study. A previous study evaluated the effect of CTA in place of DSA as the sole diagnostic and pretreatment planning study for cerebral aneurysms.[18] Although they included 223 patients in their study, only 109 patients had confirmed SAH. Also, among these 109 patients, only 88 (81%) underwent treatment based solely on CTA results. Sixteen (15%) of their patients needed DSA for further information to make a treatment decision. In our study, all of our 179 patients underwent treatment based solely on CTA findings. This makes our study unique among all studies because it represents the first large study demonstrating sensitivities and specificities approaching conventional DSA for the detection of cerebral aneurysms in the SAH patient population, while using only 16 slice CT technology.

CONCLUSION

CTA with a multi-slice scanner is a promising, safe, rapid, efficient, non-invasive technique for the detection of intracranial aneurysms in the setting of SAH. With careful systematic assessment of source images, reconstructed maximum intensity projection images and three dimensional reconstructions, CTA may be as effective and may be safer than DSA. With a submillimeter range of resolution of the distal vasculature on source images, CTA is of great value in detecting the exact size of an aneurysm. Its demonstrable increasing sensitivity and specificity makes it an ideal imaging modality to replace DSA. We are currently practicing using CTA as the only method for detection of intracranial aneurysms in the setting of SAH. Future studies will be conducted to evaluate the cost effect of this diagnostic modality, to determine the limits of resolution with multi-slice CTA technology and to develop protocols for screening for unruptured aneurysms.

Key messages

- ► CTA has been increasingly used as a means of detecting ruptured intracranial aneurysms in lieu of conventional DSA.
- ► CTA may be sensitive enough to serve as a single modality to diagnose and help guide the management of non-traumatic SAH.
- ► This study demonstrates that CTA has high sensitivity and specificity (99% sensitivity) which approaches that of conventional DSA for the detection of cerebral aneurysms in the SAH patient population.
- ► This result suggests that CTA might be an ideal imaging modality to replace DSA.

Competing interests None.

Ethics approval This study was conducted with the approval of the UMDNJ IRB Office.

Provenance and peer review Not commissioned; externally peer reviewed.

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