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REVIEW ARTICLE

Recent advances in diagnostic approaches for sub-arachnoid hemorrhage

Ashish Kumar, Yoko Kato[1], Motoharu Hayakawa[1], ODA Junpei[1], Takeya Watabe[1], Shuei Imizu[1], Daikichi Oguri[1], Yuichi Hirose[1]

Bombay Hospital Institute of Medical Sciences, Mumbai, India, [1]Fujita Health University Hospital, Toyoake, Japan

ABSTRACT

Sub-arachnoid hemorrhage (SAH) has been easily one of the most debilitating neurosurgical entities as far as stroke related case mortality and morbidity rates are concerned. To date, it has case fatality rates ranging from 32-67%. Advances in the diagnostic accuracy of the available imaging methods have contributed significantly in reducing morbidity associated with this deadly disease. We currently have computed tomography angiography (CTA), magnetic resonance angiography (MRA) and the digital subtraction angiography (DSA) including three dimensional DSA as the mainstay diagnostic techniques. The non-invasive angiography in the form of CTA and MRA has evolved in the last decade as rapid, easily available, and economical means of diagnosing the cause of SAH. The role of three dimensional computed tomography angiography (3D-CTA) in management of aneurysms has been fairly acknowledged in the past. There have been numerous articles in the literature regarding its potential threat to the conventional "gold standard" DSA. The most recent addition has been the introduction of the fourth dimension to the established 3D-CT angiography (4D-CTA). At many centers, DSA is still treated as the first choice of investigation. Although, CT angiography still has some limitations, it can provide an unmatched multi-directional view of the aneurysmal morphology and its surroundings including relations with the skull base and blood vessels. We study the recent advances in the diagnostic approaches to SAH with special emphasis on 3D-CTA and 4D-CTA as the upcoming technologies.

Key words: Aneurysm, computed tomography angiography, subarachnoid hemorrhage

Introduction

Even in presence of the modern technology and facilities at our disposal, sub-arachnoid hemorrhage (SAH) still accounts for high mortality rates. The incidence of SAH has been around 10-15 per 100, 000 person-years and has shown a downward trend off late due to early detection and management of un-ruptured aneurysms. Apart from a simple non-contrast computed tomography (NCCT) scan which is diagnostic for SAH; there are three important diagnostic modalities available at present for detection of the cause of SAH and for the pre-operative assessment of aneurysmal SAH. These are Digital Subtraction Angiography (DSA), Computed Tomography Angiography (CTA), and the Magnetic Resonance Angiography (MRA). The DSA has been the gold standard, while the MRA has clearly an advantage of not exposing the patient to radiation. Three-dimensional computed tomography angiography (3D-CTA) with multi-detector row computed tomography (MDCT) has recently provided a breakthrough in the pre-operative assessment and management of both ruptured and un-ruptured aneurysms. Inclusion of the four dimensional CT angiography (4D-CTA) to the armamentarium will help in further analysis of the probable rupture points/weak points of aneurysms and thus help to tackle them at priority.

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Address for correspondence:
Dr. Ashish Kumar, 126B, 1st Floor, MRC Building, Bombay Hospital Institute of Medical Sciences, 12, New Marine Lines, Mumbai - 400 020, India. E-mail: drashishmch@hotmail.com

The Current Technology: MRA, DSA, and the 3D-CTA

The role of MR angiography [Figure 1] has been limited in acute SAH. However, it may be found useful especially for screening patients with a positive family history of SAH. Fluid attenuated inversion recovery (FLAIR) images can detect blood pigments better than the CT in sub-acute and delayed cases of SAH.[1] In the acute SAH, however, it may not be feasible as it is often time-consuming and requires utmost patient cooperation. Also, it has an inferior resolution than the other modalities and cannot be performed in patients with metallic implants, pacemakers, and claustrophobia. The "*gold standard*" DSA, however, can be performed under local anaesthesia has got a good resolution and can demonstrate perforators and surrounding vessels near the aneurysm. It can also pick up smaller vessels (<1.2 mm) more accurately. The 3D-DSA [Figure 2] produces excellent images and adds the third dimension to the conventional angiography which is essentially *bi-planar*. The chief disadvantage is its invasiveness. Literature quotes significant stroke related morbidity due to embolic phenomenon especially in older patients with atherosclerotic vessels. The risk is between 0.1 to 2.6% in healthy patients which increases 2.5 fold in patients above 60 years with occlusive cerebrovascular disease.[2] Also, it may become difficult if the patients are uncooperative during the procedure. The other pitfall of the DSA is in demonstrating partial or complete thrombosis of an aneurysm. In comparison, 3D-CTA is least invasive. Patients undergo a helical CT scan and if SAH is detected, it is immediately followed by an angiographic study, which further undergoes post procedural reformatting in the form of maximal intensity projections (MIP), volume rendering techniques (VRT), and virtual reality images. The morphology of the aneurysm including the size, shape, direction, wall regularity, calcification, thrombosis, penetrating branches, and nearby perforators is studied extensively. Also, the relationship of the aneurysm to the bone can be best studied with the help of 3D-CTA. Thus, it becomes immensely useful in determining the correct surgical approach. The surgeon finds it helpful in pre-operative planning by rotating the image in a three dimensional way and by removing the bone slice by slice which sometimes obscures a part of aneurysm. The pictures are taken from the superior, inferior, right and left lateral, anterior and posterior aspects and also simulated for the pre-decided surgical approach. This allows visualizing the orientation of aneurysms and nearby vessels before the surgery from the desired approach and can help in certain modifications to it, if needed. The well known advantages of 3D-CTA are its non-invasiveness and rapid acquisition, while providing good resolution. Also, the calcifications and thrombosis of the lumen can be better appreciated. The chief disadvantages are the potential to cause nephrotoxicity and suboptimal resolution for very small vessels (<1.2 mm). Also, post procedural reformatting from the raw data is required.

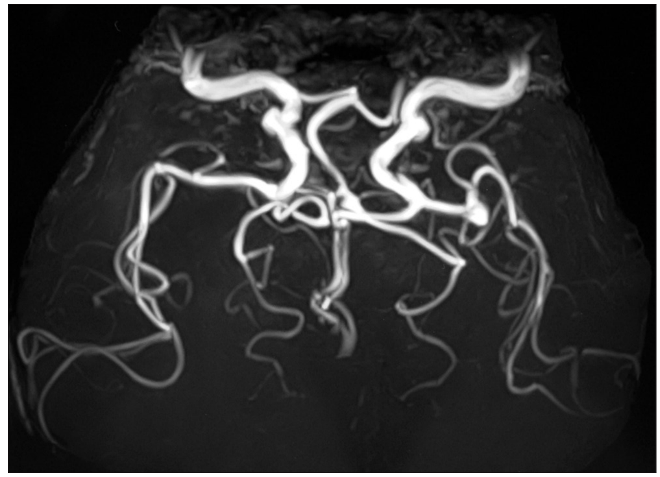

Figure 1: MRA showing left MCA bifurcation aneurysm

Figure 2: 3D-DSA showing ophthalmic ICA aneurysm

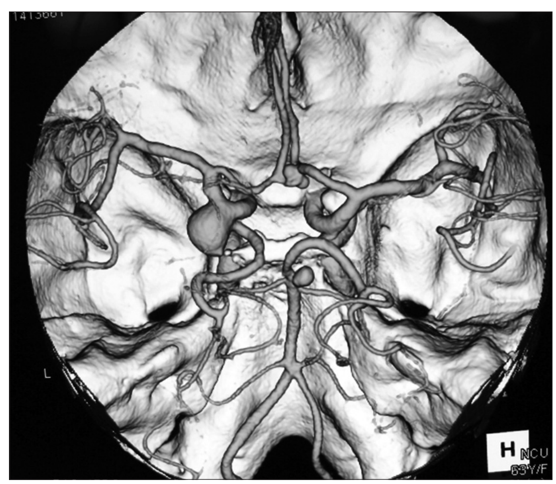

Figure 3: 3D-CTA showing p-com, a-com and basilar aneurysms in one patient with fetal posterior circulation

In 3D-CTA, complex aneurysms involving the anterior communicating artery, posterior communicating artery, and internal carotid artery [Figure 3] can be seen with excellent resolution and their relationship to skull base, anterior clinoid, or any nearby vessel can be studied [Figure 4]. This may be particularly true in cases of middle cerebral artery aneurysms [Figure 5]. Operative simulation is done before the surgery. This is done after subtracting the proposed craniotomy bone from the image and rotating it as for example, a pterional craniotomy [Figure 6]. This helps the surgeon to orient himself regarding the position of the neck and dome of the aneurysm. In cases of large ophthalmic aneurysms, even the extent of anterior clinoid drilling can be pre-assessed by bony subtraction of the anterior clinoid [Figure 7]. Large cavernous segment ICA aneurysms can

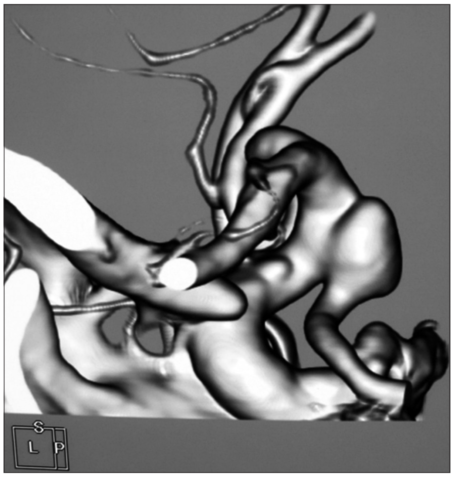

Figure 4: Lateral view showing p-com artery arising from the aneurysmal dome and relation of ICA with ACP

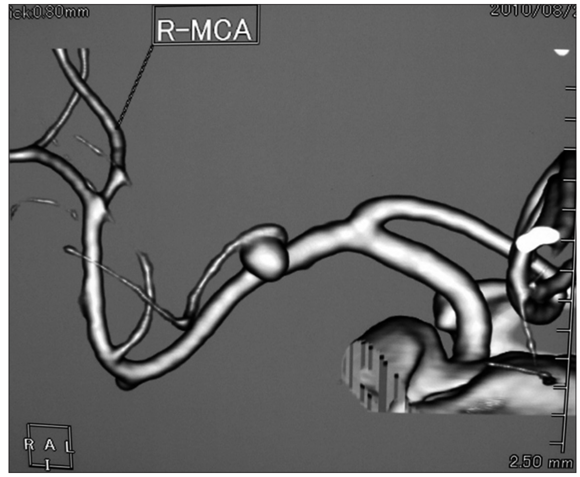

Figure 5: Middle cerebral artery (M-1 segment) aneurysm and a proximal branch adhered to the dome seen from anterior projection

Figure 6: Simulation for a pterional craniotomy to approach post communicating ICA aneurysm

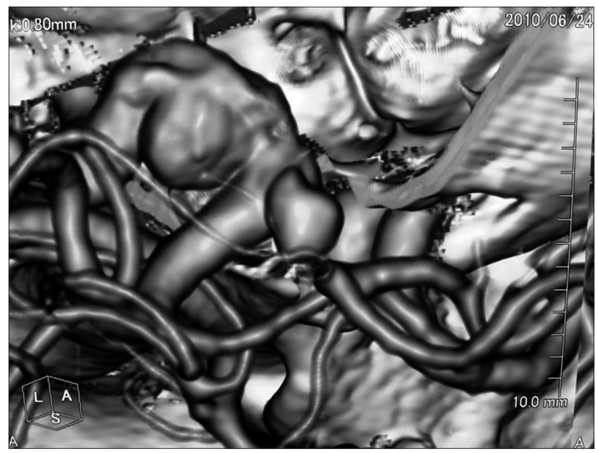

Figure 7: Antero-lateral view showing ophthalmic segment ICA aneurysm with ipsilateral ACP subtraction; another cavernous segment ICA aneurysm seen

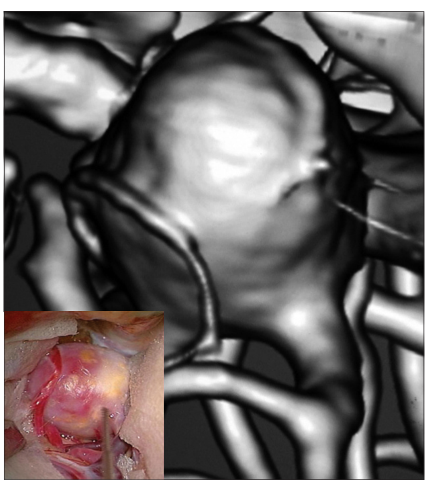

Figure 8: A large MCA aneurysm with two perforators stuck to its wall as seen on 3D-CTA with good intra-operative correlation (inset)

be easily visualized without any bone artefact. A large MCA aneurysm with small perforators stuck on its wall could be correlated well during the surgery [Figure 8].

The Future Technology: 4D-CT Angiography

4D-CTA is the most recent addition to the imaging techniques at hand. The fourth dimension is the *phase data* merged with the conventional 3D-CTA. Here, electrocardiographically (ECG) gated multisection helical CT images/320 row area detector CT (ADCT) images are obtained. CT angiography is performed over one or two cardiac cycles while acquiring ECG data. The data obtained for each R-R interval is subdivided in 20 parts and volume reconstruction is performed for each part to detect the pulsations of aneurysms. This reconstruction is a method for minimizing cardiac motion artifacts during the scanning. This can help in detection of the weaker points or blebs of the aneurysmal wall which demonstrate increased pulsations and can help in predicting the site of rupture in aneurysms. Still, the artifacts may pose significant hindrance in assessing these pulsations. More trials are required to demonstrate its actual utility in aneurysms and as a modality to assess residual necks post clipping owing to the superadded clip artifacts.

Discussion

Siddiqui *et al*., reviewed literature about the diagnostic efficacy of 3D-CTA over DSA and found CTA extremely useful in all but few occasions.[3] In a recent paper by Nagai and Watanbe,[4] there is a detailed analysis regarding the role of 3D-CTA in the ruptured cerebral aneurysms. Aneurysm clipping was performed using only 3D-CTA in place of DSA to evaluate the suitability of multi-detector CT (MDCT) angiography for pre-operative evaluation and to point out all the necessities required for 3D CTA images. The surgeon himself formatted the CTA and rotated the 3D image for his orientation. The sphenoid ridge was removed partially to simulate the surgical view. Any patient where the CTA was negative, conventional DSA was performed. Thereafter, all anterior circulation aneurysms were taken directly for surgery, while posterior circulation ones were referred for coil embolization. Twenty five patients underwent craniotomy and four were treated by coil embolization. One patient with no aneurysm on CTA underwent DSA twice. No aneurysm was detected. Two parameters were assessed in the study. One, the sensitivity of CTA in depicting aneurysms in patients of SAH and other was the time between admission and entering the operating room. The sensitivity of 3D-CTA was 100% and shapes of all the aneurysms depicted by it were validated intra-operatively. The false negative rate was 0%. The mean operation waiting time was 2.8 hours with the shortest being 1.5 hours. The mean time in the DSA group was 4.1 hours. Re-bleeding occurred in 1 of the 20 patients which occurred 45 minutes after the admission. A total of 21 patients had good recovery, 1 had moderate disability, and 2 became severely disabled, while 1 patient died due to vasospasm and pneumonia. Almost 60% of aneurysm bleeding occurs within six hours after the first SAH and DSA within first six hours is associated with a risk of re-bleeding (2-5%). Thus, CTA in this interval becomes extremely useful and early surgery can be performed leading to lesser chances of re-bleeding. Sadamasa *et al*.[5] did a retrospective analysis of the mortality rates of patients with SAH for a 10-year period. The overall mortality was 18.1%, while the average fatality rate had a downward slope from 24.2% in 1999-2002 to 15.9% in 2005-2008 ($P=0.016$). Amongst various factors like improved management of patients and surgical techniques, one of the factors was transition from DSA to less invasive 3D-CTA. In the earlier group, 55.3% patients underwent diagnostic DSA and 23% patients were diagnosed from CTA. While in the latter group, 70% patients underwent CTA and only 13.7% patients underwent DSA ($P<0.0001$). This article lays an important foundation in the changing trends in diagnostic protocols over the years. The transition from the conventional DSA has been linked to early surgery and thus improved outcomes. Another modification of the 3D-CTA is the virtual reality (VR) system which studies the aneurysmal morphology and its relationships to other vessels. Mo *et al*.[6] studied 28 aneurysms over a three-year period. They concluded that the VR system generated clear and vivid 3-D virtual images. It displayed the location and size of the aneurysms and their precise anatomical spatial relations to the parent arteries and skull. The location, size, and shape of the aneurysms and their relationship with the adjacent vessels were similar between 3-D virtual image and 3D-DSA, which is a better modulation of the bi-planar DSA. Khan *et al*.[7] also echoed the excellent role of 3D-CTA in identifying cerebral aneurysms, their surrounding vascular anatomy, the presence of vasospasm, and whether the aneurysm had a clearly definable sac and neck. They found it to be 92.3% sensitive and found it to be extremely useful in preoperative planning and post-operative follow-up. As the re-bleeding rates of aneurysms lead to mortality rates as high as 80%, there should be no false negative result leading to death by non-diagnosis. Kallmes *et al*.,[8] however, thought that the resolution of CTA (0.35-0.5 mm) is less than that of DSA (0.2-0.3 mm) and thus there are significant chances of missing an aneurysm of smaller vessels like *anterior choroidal artery* which can prove detrimental for the patient. All these negative CTAs should be followed by DSA so that nothing remains undiagnosed. Agid *et al*.,[9] found a sensitivity of 98% with 100% specificity and 100% positive predictive value. They validated CTA for *triaging* patients and selecting the best treatment option for them (clipping vs coiling). A retrospective study analyzed the 53 clipped aneurysms during a six-year period and compared the 3D-CTA and DSA in detecting post clipping neck remnants, residual aneurysms, and parent vessel occlusion.[10] Computed tomography angiograms were independently reviewed by two blinded neuro-radiologists and were re-reviewed by one at least four months later. Digital subtraction angiograms were reviewed in a similar manner by a third blinded neuro-radiologist. On DSA, 35 were completely obliterated, 10 had neck remnants, and 8 had residual aneurysms. The ability of CTA to detect residual aneurysms versus complete obliterations was excellent (mean sensitivity, 88%; specificity, 100%; positive predictive value (PPV), 100%; negative predictive value (NPV), 98%). However, the ability of CTA to detect neck remnants versus complete obliterations was poor (mean sensitivity, 20%; specificity, 99%; PPV, 83%; NPV, 81%). The CTAs were also good at detecting parent vessel occlusion (mean sensitivity, 88%; specificity, 97%; PPV, 75%; NPV, 99%). Authors proved the superiority of conventional angiography over CTA in post operative assessment of clipped aneurysms and restricted the use of CTA in following the patients of residual aneurysms after the initial DSA. Hayakawa *et al*. mentioned the technique and the rationale behind the 4D-CTA after analyzing 23 patients with different ruptured aneurysms.[11] Four patients showed pulsation of an aneurysmal bleb. Two of these patients underwent clipping and the ruptured site was seen to match the pulsatile bleb detected on the 4D-CTA pre-operatively.

Summary

The recent advances in the angiography methods in management of SAH have led to improved clinical outcomes. The use of MRA may be limited to chronic SAH cases and for screening the patients with a strong family history. DSA still remains choice of investigation at many centres although 3D-DSA can also be useful in delineating the aneurysmal shape and morphology. It certainly has the best of resolution till date and can pick up even smallest of the vessels and compensates for the *biplanar* conventional DSA. Also, for examining the 'dynamic' cross circulation, diagnostic, and therapeutic treatment of vasospasm (chemical angioplasty) DSA may be found useful. DSA remains a procedure of choice for post operative assessment of clipped aneurysms and its superiority over CTA in this particular scenario is proven. In case of 3D-CTA not being able to detect an aneurysm, the patient should undergo a DSA. However, the major limitations are its invasiveness and the inability to detect thrombosed aneurysms. After the analysis of the recent literature, we found the rapidly emerging 3D and 4D CT angiography may be found extremely useful in comparison. The rapidity with which a CTA can provide the result within six hours of the ictus and thus shorten the time to surgery cannot be ignored. With the recent multi-detector CT (MDCT) scanners, excellent resolution can be achieved and even smaller vessels can be visualized too. However at some centres, the resolution may remain a major limitation in detecting small aneurysms and perforators. In those cases, where there is a doubt, one can always perform the conventional angiography so that nothing remains undiagnosed and thus it is better used as a therapeutic procedure for coiling the aneurysms under general anaesthesia once the diagnosis is confirmed on CTA. Hence, patients can avoid two invasive procedures. Not to forget about the key point of the surgeon himself doing the reconstruction to get 'the surgeon's view'. This should help him in understanding the anatomy in a better way.

At present, there seems to be a debate regarding the ideal investigation for pre-operative assessment of aneurysms in SAH after emergence of less invasive 3D-CTA. It can be safely concluded, however, that the first investigation can be 3D-CTA owing to the ease and its widespread availability and only if no aneurysm is detected, the patient should undergo conventional angiography (3D-DSA preferably). The role of MRA remains limited and the role of 4D-CTA has to be studied more extensively with randomized trials so that its potential is explored to maximum and in the future, we may see its more widespread application.

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