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Non-contrast 3D time-of-flight magnetic resonance angiography for visualization of intracranial aneurysms in patients with absolute contraindications to CT or MRI contrast

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Abstract

The preoperative evaluation in patients with intracranial aneurysms typically includes a contrast-enhanced vascular study, such as computed tomography angiography (CTA), magnetic resonance angiography (MRA), or digital subtraction angiography. However, there are numerous absolute and relative contraindications to the administration of imaging contrast agents, including pregnancy, severe contrast allergy, and renal insufficiency. Evaluation of patients with contrast contraindications thus presents a unique challenge. We identified three patients with absolute contrast contraindications who presented with intracranial aneurysms. One patient was pregnant, while the other two had previous severe anaphylactic reactions to iodinated contrast. Because of these contraindications to intravenous contrast, we performed non-contrast time-of-flight MRA with 3D reconstruction (TOF MRA with 3DR) with maximum intensity projections and volume renderings as part of the preoperative evaluation prior to successful open surgical clipping of the aneurysms. In the case of one paraclinoid aneurysm, a high-resolution non-contrast CT scan was also performed to assess the relationship of the aneurysm to the anterior clinoid process. TOF MRA with 3DR successfully identified the intracranial aneurysms and adequately depicted the surrounding microanatomy. Intraoperative findings were as predicted by the preoperative imaging studies. The aneurysms were successfully clip-obiterated, and the patients had uneventful post-operative courses. These cases demonstrate that non-contrast imaging is a viable modality to assess intracranial aneurysms as part of the surgical planning process in patients with contrast contraindications. TOF MRA with 3DR, in conjunction with high-resolution non-contrast CT when indicated, provides adequate visualization of the microanatomy of the aneurysm and surrounding structures.

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Conflicts of Interest/Disclosures

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Keywords

Aneurysm; Contrast; Intracranial; MRI; Pregnancy; Time of flight

1. Introduction

The modern preoperative evaluation in patients with intracranial aneurysms typically includes CT or MR angiography (CTA or MRA) or digital subtraction angiography (DSA) ¹ for detailed visualization of the microvasculature and surrounding microanatomy ². All of these techniques require the administration of intravenous (IV) contrast, thus making preoperative evaluation in patients with contraindications to contrast agents an area of uncertainty. Prior severe contrast allergy is an absolute contraindication to the use of iodinated CT contrast agents or gadolinium MRI contrast agents, and occurs in approximately 0.1% of the population. Anaphylactic reaction to contrast results in fatalities in 1 in 75,000 administrations ^{3,4}. Pregnancy is an important absolute contraindication to the use of MRI gadolinium contrast due to its possible teratogenicity ⁵, while avoidance of CT scans is preferable in pregnant women because of the risks of radiation exposure to the developing fetus. Additionally, chronic kidney disease, defined as a glomerular filtration rate < 60 mL/min/1.73m², affects approximately one-third of patients above age 64, and is a relative contraindication ⁶ for both CT and MRI contrast. Patients with absolute or relative contraindications to CT or MRI contrast therefore represent about 20% of the overall population ⁶. The ability to successfully use non-contrast imaging modalities in these patients is critical to ensuring a safe preoperative evaluation.

There are several reports of the use of alternative modalities for the evaluation of abdominal aortic aneurysms, including non-contrast CT scans, carbon dioxide aortography, and intravascular ultrasound ^{7,8}. These have been used successfully as the sole preoperative imaging methodologies prior to the repair of aortic aneurysms. However, to our knowledge, there are no such reports for the successful sole use of non-contrast methods for the preoperative evaluation of intracranial aneurysms in the literature.

Time of flight (TOF) MRA is a modality that has been investigated within the past two decades in the diagnosis of intracranial aneurysms ⁹⁻¹² and can be performed with or without gadolinium enhancement. TOF imaging exploits the differential effects of rapid, slice-selective, radiofrequency (RF) pulses on stationary *versus* flowing protons. The repetitive RF pulses suppress the signal from saturated stationary protons within the slice but enhance the signal from fully magnetized protons flowing into the slice, leading to high flow-related contrast. Rapidly flowing arterial blood is not saturated because it sees a limited number of magnetic pulses compared to the surrounding tissue and is thus highlighted against a saturated background.

Prior studies have demonstrated that TOF MRA may be as accurate as contrast-enhanced MRA and CTA in detecting intracranial aneurysms ¹². Indeed, ongoing technical refinements have improved the quality of cerebral TOF MRA, including the use of 1) multiple overlapping thin slab acquisitions and variable flip-angle excitation to reduce progressive saturation of flowing spins in the acquisition volume; 2) fat saturation and magnetization transfer pulses to further suppress the signal from stationary tissues; and 3) higher magnetic field strengths (e.g. 3T) and parallel imaging to increase signal-to-noise ratio, increase spatial resolution, and decrease imaging time. However, previous studies have focused on the use of TOF MRA as a screening modality, with further characterization done through contrast modalities prior to surgical intervention ⁹⁻¹².

Recently, three-dimensional reformatting (3DR) of TOF MRA has led to improved resolution of the intracranial vasculature. TOF MRA with 3DR has been utilized for radiosurgical preoperative planning for arteriovenous malformation (AVM) treatment¹³, but to date no studies have examined its potential as a sole imaging modality in the preoperative planning for aneurysm repair.

Given the evidence for the accuracy of TOF MRA in detecting intracranial aneurysms, we thus asked whether non-contrast TOF MRA with 3DR could be successfully used as the sole preoperative surgical planning modality for intracranial aneurysm repair in patients with contrast contraindications.

2. Methods

2.1 Imaging

MRA was performed on a 1.5 T magnet, (Case 1: Magnetom Avanto, Siemens AG, Berlin, Germany; Cases 2 and 3: Signa HDxt, GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom). TOF MRA was obtained using 3D gradient echo sequences (Case 1: TE 7.15 ms, TR 24 ms, flip-angle 25°, multiple overlapping thin slab acquisition, in-plane pixel spacing 0.625 mm, slice spacing 0.8 mm, slab thickness 28.8 mm; Cases 2 and 3: TE 3.2 ms, TR 25 ms, flip-angle 20°, with variable flip-angle excitation and magnetization transfer contrast, in-plane pixel spacing 0.352 mm, slice spacing 0.6 mm). No gadolinium contrast was administered.

2.2 3D reconstruction

The acquired image data sets were transferred to the GE Advantage workstation (GE Healthcare) where the 3D images were reconstructed with a 1024 × 1024 matrix by maximum intensity projection (MIP) and volume rendering (VR) using the associated 3D software package.

3. Case reports

3.1 Case 1

A 42-year-old woman with a family history significant for four close relatives (sister, father, paternal aunt, and paternal grandmother) with ruptured intracranial aneurysms presented at 27 weeks of pregnancy complaining of progressively worsening headaches and an episode of loss of consciousness. A non-contrast MRI done at an outside hospital at the time of her syncopal episode revealed what appeared to be an unruptured left posterior communicating artery aneurysm. She had no other significant history and her neurological exam was unremarkable, as was the rest of her physical exam, other than her gravid uterus. This MRI unfortunately did not provide adequate visualization of the microanatomy of the aneurysm for surgical planning. Because of her pregnancy, both CT scans and MRI with gadolinium contrast were contraindicated. We performed a non-contrast TOF MRA with 3DR as described in the methods (Fig. 1), which demonstrated an unruptured 6–7 mm bilobed saccular aneurysm near the origin of the left posterior communicating artery, as well as an unruptured 3–4 mm saccular aneurysm near the origin of the right ophthalmic artery. Given her family history and risk of mortality from subarachnoid hemorrhage during pregnancy, we recommended treating the larger aneurysm without further delay, prior to delivery. Endovascular coiling would have involved radiation and contrast exposure, and thus open clipping was deemed the best option. A left pterional craniotomy was performed to access the left posterior communicating artery aneurysm. Intraoperatively, the aneurysm was observed to be impaled upon the tentorial edge, producing the bi-lobed appearance noted on imaging. The aneurysm was clipped without complication. The smaller right ophthalmic

region aneurysm was also identified, although there was insufficient proximal control of the internal carotid artery from this approach to safely clip it. We therefore deferred intervention to a later date with a planned right-sided approach. The patient remained neurologically intact postoperatively and was discharged home without complications.

3.2 Case 2

A 54-year-old woman presented after an unruptured right paraclinoid region aneurysm was found incidentally on an MRI performed at an outside hospital for evaluation of suspected central diabetes insipidus. The study was otherwise normal except for this incidental finding. She had no other significant history and her neurological exam was intact. The patient had a known previous anaphylactic reaction to IV iodinated contrast, leading us to perform a non-contrast TOF MRA with 3DR (Fig. 2a) to avoid a possible adverse reaction to gadolinium contrast. This study demonstrated an unruptured 6 mm saccular aneurysm arising from the right paraclinoid internal carotid artery (ICA), approximately at the level of the origin of the ophthalmic artery. To better understand the relationship of the aneurysm to the anterior clinoid process, we also obtained a high-resolution non-contrast CT (Fig. 2b), which revealed that the aneurysm had not eroded the anterior clinoid. Endovascular coiling was precluded because of her severe contrast allergy, and we thus proceeded with open clipping. The aneurysm was approached via a standard right pterional craniotomy, where it was identified as predicted by imaging (Fig. 2c, d), and successfully clipped. The patient experienced a partial fourth nerve palsy postoperatively, which had resolved by the time of her three month follow-up.

3.3 Case 3

A 40-year-old woman with a long smoking history and known severe IV contrast allergy had an MRI performed at an outside facility during the work-up for persistent headaches. This study showed an abnormality in the region of the right posterior communicating artery that was difficult to distinguish. Given her contrast allergy, we performed a non-contrast TOF MRA with 3DR (Fig. 3). This study demonstrated a 4 mm unruptured aneurysm at the origin of the right posterior communicating artery. Considering her potentially increased risk of aneurysmal rupture given her smoking history, definitive treatment of the aneurysm was recommended. Endovascular coiling was contraindicated given her severe contrast allergy, and we therefore proceeded with open clipping through a right pterional craniotomy. Intraoperatively the aneurysm was identified with a geometry and relationship to the ICA and posterior communicating artery as predicted by the 3D TOF MRA. The patient recovered uneventfully and was discharged without complications.

4. Discussion

We report three patients with absolute contraindications to the administration of contrast agents in whom we performed TOF MRA with 3DR without gadolinium contrast prior to successful open surgical clipping of intracranial aneurysms. While contrast imaging will likely remain the mainstay of preoperative intracranial aneurysm evaluation, these cases demonstrate that non-contrast imaging can serve as a viable modality to assess intracranial aneurysms as part of the surgical planning process in the uncommon instance of contrast contraindication. In each case, TOF MRA with 3DR provided adequate visualization of the microanatomy of the aneurysm and surrounding structures. Given the importance of timely repair of intracranial aneurysms to prevent spontaneous rupture, we demonstrate that non-contrast imaging may present a viable option for safe open surgery in patients with contrast contraindications. Whereas absolute contraindications are relatively rare, up to 20% of the population may have relative contraindications⁶, making them candidates for consideration of this option.

Pregnancy is one contraindication that poses particular difficulty, because all CT modalities are contraindicated except under emergent situations, as is the use of gadolinium contrast agents for MRI. Ionizing radiation from CT scanning poses a risk to the developing embryo or fetus primarily during the first and second trimesters. During the first 14 days, ionizing radiation can induce the complete loss of the developing embryo¹⁴. From that time until the eighth week after conception, during the period of organogenesis, it can induce fetal growth restriction and congenital malformations, including microcephaly and mental retardation¹⁵. After approximately 26 weeks, the fetus is more resistant to the teratogenic effects of ionizing radiation¹⁶, but the risks and benefits of its use should still be considered carefully. Iodinated contrast agents cross the placenta and produce transient effects on the developing fetal thyroid and are thus generally avoided. Gadolinium similarly crosses the placenta and may accumulate in fetal tissues indefinitely with unknown effects^{17,18}.

Thus non-contrast MRI is the only modality without potential fetal risk for the evaluation of unruptured intracranial aneurysms in these patients. Numerous studies have suggested that aneurysm growth rate and rupture risk increase throughout the course of pregnancy¹⁹. Because intracranial (subarachnoid and intraparenchymal) hemorrhage, the majority of which are attributable to ruptured aneurysms, accounts for 5–12% of maternal deaths during pregnancy²⁰, the magnitude of this problem is significant. Indeed, the majority of pregnant women with intracranial aneurysms report that the benefits of surgical intervention during pregnancy outweigh the risks²⁰. Thus, TOF MRA provides an important imaging modality without risk to the fetus that can allow for safe surgical evaluation of intracranial aneurysms. Notably, AVM do not appear to have the same increased rupture risk, and treatment is thus generally deferred until after delivery²⁰.

Allergic reactions are another major contraindication to the use of imaging contrast. Importantly, the severity of anaphylactic reactions to contrast media is not dose-dependent, and clinical consequences are unpredictable, ranging from cutaneous rashes to catastrophic shock²¹. The severity of prior reactions does not correlate well with the severity of future reactions²¹. Premedication with prednisone, diphenhydramine, methylprednisolone, or a combination thereof is possible, although there are numerous examples of premedication failure with resultant death²². The American College of Radiology currently recommends the use of alternative modalities whenever possible²².

The use of contrast agents in patients with chronic renal insufficiency or renal failure is another substantive challenge. Contrast-induced nephropathy is a complication in 30–50% of patients with serum creatinine above 2.5 mg/dL, despite prophylactic pretreatment with hydration or N-acetylcysteine²³. Each gadolinium study presents a 2.4% risk for developing nephrogenic systemic sclerosis in patients with end-stage renal disease²⁴. Thus, both iodinated contrast agents and gadolinium present significant risks in patients with renal disease and should be avoided whenever possible.

Non-contrast modalities are therefore imperative in a number of patient populations. However, while our results demonstrate that TOF MRA with 3DR can be a viable method to investigate intracranial aneurysms preoperatively, there are still several reservations that present limitations to its widespread use. One of the biggest challenges is accurately imaging areas with aberrant flow patterns²⁵. Low blood flow may cause signal loss due to spin saturation, while turbulent blood flow may cause signal loss due to intravoxel spin phase dispersion. These flow-related artifacts may limit our ability to accurately assess the anatomy of partially thrombosed or otherwise complex aneurysms. Sizeable hematomas may also distort the view of aneurysms or even altogether obscure underlying aneurysms in a way that conventional DSA would not²⁵. These limitations must thus be considered in all cases when using TOF MRA for the evaluation of intracranial aneurysms.

There are several methods for 3D reconstruction of TOF MRA (and other modalities, including CTA), including maximum intensity projections (MIP) and volume renderings (VR). Each of these methods has its advantages and disadvantages. There is evidence that VR more accurately depict three-dimensional relationships, while MIP may not because of the particularities of the processing in the MIP algorithm²⁶. VR also allow for greater definition of the surrounding soft tissues, muscle and bone, while these are eliminated on MIP²⁶. However, MIP may display smaller branch vessels better than VR²⁶. There is thus room for the use of both projections in the evaluation of intracranial aneurysms.

5. Conclusion

TOF MRA with 3DR represents a useful imaging modality for investigating the microanatomy of intracranial aneurysms in patients with contraindications to contrast media. The number of patients with absolute contraindications is small, but these techniques may be readily applied in populations with relative contraindications, especially in the presence of other complicating comorbidities. We observed that the microanatomic visualization provided by this method provided sufficient detail of the geometry of the aneurysm and its relationship to surrounding structures to enable accurate preoperative planning. We therefore recommend considering this option in patients in whom the risk/benefit profile of contrast media administration is concerning.

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Fig. 1.

Volume rendering of time-of-flight magnetic resonance angiography from Case 1 showing an unruptured 6–7 mm bilobed saccular left posterior communicating artery aneurysm (solid arrow) and an unruptured 3–4 mm saccular aneurysm of the right ophthalmic artery (dashed arrow).

L A1; first segment of the left anterior cerebral artery, L ICA: left internal carotid artery, L M1: first segment of the left middle cerebral artery, L P1: first segment of the left posterior cerebral artery, R ICA: right internal carotid artery, R M1: first segment of the right middle cerebral artery.

Fig. 2.

(a) Volume rendering of time-of-flight magnetic resonance angiography and associated non-contrast CT from Case 2 along with intraoperative images showing an unruptured 6 mm saccular aneurysm (arrow) arising from the right paraclinoid region internal carotid artery.

(b) High-resolution non-contrast head CT scan showing symmetric anterior clinoid processes (arrows) with no erosion from the aneurysm. (c) The intraoperative image just prior to placement of the permanent clip across the aneurysmal neck showing the anatomy of the aneurysm (arrow) with respect to the optic nerve (CNII), ophthalmic artery (OA), anterior clinoid process, and internal carotid artery was consistent with our expectations from the preoperative imaging. (d) Intraoperative photograph showing placement of the permanent clip (arrow) across the neck of the aneurysm.

R ICA: right internal carotid artery, R M1: first segment of the right middle cerebral artery, R P1: first segment of the right posterior cerebral artery.

Fig. 3.

Volume rendering of time-of-flight magnetic resonance angiography from Case 3 showing a 4 mm unruptured aneurysm at the origin of the right posterior communicating artery (arrow). R A1: first segment of the right anterior cerebral artery, R ICA: right internal carotid artery, R M1: first segment of the right middle cerebral artery, R P1: first segment of the right posterior cerebral artery, R PCOM: right posterior communicating artery.