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3D T1-weighted black blood sequence at 3.0 Tesla for the diagnosis of cervical artery dissection

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ABSTRACT

Objective: We aimed to investigate the value of three-dimensional (3D) T1 volumetric isotropic turbo spin echo acquisition (VISTA) in the diagnosis of cervical artery dissection (CAD).

Methods: We prospectively included patients who were suspected as having a CAD within 1 month of onset. For T1 VISTA, the diagnosis of the dissection was based on the presence of intramural high-signal, intimal flap, double lumen and aneurysmal dilation. The final diagnosis of dissection was based on the clinical history, physical examination, and all of the imaging tests.

Results: A total of 46 patients were included in this study. The final diagnosis of CAD was made for 21 patients. Diagnosis of dissection was made for 20 of the 21 patients after assessing T1 VISTA. A definitive diagnosis of dissection was not made for 5 patients (including 3 patients with digital subtraction angiography) before the T1 VISTA examination. The sensitivity and specificity for T1 VISTA were 95.2% (95% CI, 76.2% to 99.9%) and 100% (95% CI, 86.3% to 100%), respectively. The agreement between the two researchers for T1 VISTA for diagnosis of CAD was very good (k=0.91). For patients without acute artery occlusion, all of them had a definite conclusion with or without dissection by T1 VISTA (n=29). However, for 17 patients with acute artery occlusion, the possibility of dissection could not be excluded for 6 of them by T1 VISTA (p=0.001).

Conclusions: 3D T1 VISTA at 3.0 Tesla was useful in the diagnosis of acute CAD. However, for some patients with total occlusion of the artery without typical imaging features of dissection, the unequivocal distinction between intramural haematoma and intraluminal thrombus may be not adequate by T1 VISTA alone. Future studies should investigate whether a follow-up scan, a contrast-enhanced imaging or an optimal VISTA technique could be useful.

INTRODUCTION

Spontaneous cervical artery dissection (CAD) accounts for only ~2% of all ischaemic strokes, but it accounts for 10–25% of ischaemic strokes in young adult patients.[1] CAD can cause ischaemic symptoms typically through two mechanisms, which are thromboembolic and haemodynamic compromises.[2 3] The early and reliable diagnosis of CAD is highly important for treatment decision-making in the era of precision medicine.[4 5]

Conventional angiography has long been the gold standard for the diagnosis of CAD.[6] However, this method is invasive and does not have the advantage of demonstrating mural haematoma.[7] With the advent and development of MRI techniques, like MR angiography (MRA) combined with an axial two-dimensional (2D) fat-saturated spin echo T1-weighted sequence has shown an evident advantage in the diagnosis of CAD.[1 8–10] However, the axial 2D T1-weighted sequence has several limitations. It is time-consuming to cover all arteries and shows poor performance for the arteries with a tortuous course.[11 12]

The three-dimensional (3D) isotropic T1-weighted spin echo sequence can overcome the limitations of a 2D sequence.[13 14] Some researchers have found that a 3D black blood T1-weighted sequence of volumetric isotropic turbo spin echo acquisition (VISTA) offers similar or more information than a 2D T1-weighted spin echo sequence.[15–17] We aimed to investigate the value of a 3D T1 VISTA sequence at 3.0 T for the diagnosis of CAD. We also investigated the limitations of 3D T1 VISTA in the diagnosis of CAD.

METHODS

In reporting the current study, the standards for reporting diagnostic accuracy studies were followed.[18] This study was not publicly registered.

Participants

Between September 2014 and February 2016, we prospectively included consecutive patients who were suspected as having an acute CAD with the following symptoms or

signs: Horner's syndrome, unusual neck pain and/or headache, cranial nerve palsy and tinnitus. The CAD was considered acute if the duration of symptoms was ≤30 days. Patients who had the above signs or symptoms, particularly if in combination and/or associated with a cerebral or retinal ischaemia, were highly suspected as having a CAD. Patients who were suspected as CAD by imaging tools of MRA or ultrasound were also included. This study was approved by the institutional review board of the first hospital of Jilin University. Written consent forms were obtained from all patients.

Imaging protocols

A 3D T1 VISTA examination was performed on all patients who were included in this study. At least one examination of angiography including MRA, CT angiography (CTA), and digital subtraction angiography (DSA) was performed on each patient. A 3D T1 VISTA protocol was performed using a 3.0 Tesla scanner (Philips Ingenia, Eindhoven, The Netherlands) with a standard 8-channel head/neck coil. The following parameters were used for the 3D T1 VISTA sequence: an oblique coronal plane acquisition, spectral adiabatic inversion recovery fat saturation mode, repetition time (TR)/echo time (TE)=350 ms/19 ms, field of view= 280×199×120 cm^3, 400×284 matrix, variable refocusing flip angle, slice interval=0; voxel size=0.7×0.7×0.7 cm^3, oversample factor=1.5, and number of excitations=2. The acquisition time was 3 min and 38 s.

Data analysis

The analysis of 3D T1 VISTA results was performed by two experienced neuroradiologists who were blinded to all of the patient information and the final diagnosis. Images along the short and long axes of the arteries could be reconstructed at the workstation. For 3D T1 VISTA, the diagnosis of the dissection was based on the presence of the following features: intramural high signal, particularly if it is a semilunar hyperintense signal; intimal flap and/or double lumen; and aneurysmal dilation.[14] The final diagnosis of the dissection was based on the clinical history, physical examination, and all of the imaging tests by two experienced neurologists. For conventional imaging tests, the imaging signs for diagnosis of CAD including double lumen, intimal flap, pearl and string sign, string sign, and tapered occlusion.[15] Disagreement between the two observers were resolved be consensus.

SPSS V.19.0 (IBM, West Grove, Pennsylvania, USA) was used to perform the analysis. Since no gold standard for the diagnosis of CAD was available, the final diagnosis results were chosen to be the reference standard to calculate the sensitivity and specificity (including the corresponding 95% CI) for 3D T1 VISTA. Interobserver agreement for 3D T1 VISTA was examined by using the κ-coefficient of agreement.[19] Fisher's exact test was used for count data. The level of statistical significance was set at $p<0.05$.

RESULTS

A total of 46 patients were included in this study. 3D T1 VISTA examination was performed on each of them. The final diagnosis of the dissection was made for 21 patients (6 females) (table 1). There were eight patients with single carotid artery dissection and nine patients with single vertebral artery dissection. One patient had bilateral carotid artery dissections and bilateral vertebral artery dissections. Three patients had bilateral vertebral artery dissections. One patient with vertebral artery dissection presented with neck pain accompanied by right-sided weakness and left-sided numbness (Brown-Séquard syndrome) (patient number 11). The median age of patients with dissection was 38 years (range 27–74 years old).

The median time between disease onset and the examination with 3D T1 VISTA was 11 days with a range of 3–26 days for patients with dissection. Diagnosis of dissection was made for 20 patients after assessing the 3D T1 VISTA data alone by two researchers. Among these 20 patients, the diagnosis of dissection was not made for five (including 3 patients with DSA) of them before the examination with T1 VISTA. The sensitivity and specificity for 3D T1 VISTA were 95.2% (95% CI, 76.2% to 99.9%) and 100% (95% CI, 86.3% to 100%), respectively. The agreement between the two researchers for T1 VISTA for diagnosis of CAD was very good (k=0.91).

Patient number 1 presented with headache and transient motor weakness on the right side (table 1). Duplex ultrasonography and a subsequently CTA showed stenosis and possible dissection of the right vertebral artery, which was confirmed by 3D T1 VISTA (figure 1). T1 VISTA images of the other 18 patients all showed typical crescent-shaped hyperintense signals surrounding the lumen (patients number 2–19).

Patient number 20 presented with aphasia and motor weakness on the right side. Duplex ultrasonography of the left internal carotid artery at 15 days of onset showed a double lumen and intima, which suggested the aetiology was dissection. However, there was no typical crescent-shaped hyperintense signal on VISTA at 26 days of onset, one of the two researchers insisted that the definite diagnosis of dissection could not be made by T1 VISTA alone (figure 2).

Patient number 21 presented with dizziness, headache, and hemiplegia. 3D T1 VISTA at 5 days of onset showed high-signal intensity of the left vertebral artery (figure 3). One of the reconstructed images along the short-axis of left vertebral artery showed a non-typical crescent-shaped hyperintense signal. One researcher suggested that it was unreliable to make a diagnosis of dissection based on the images of T1 VISTA. However, a repeat scan of T1 VISTA at 23 days of onset showed the recanalisation of occlusion and a residual intramural haematoma, which confirmed the diagnosis of dissection.

For patients without artery occlusion, all of them had a definite conclusion with or without dissection by VISTA (n=29). However, for 17 patients with artery occlusion,

Table 1 Characteristics of patients with a final diagnosis of dissection

Patient	Age	Symptoms	Acute infarction	Location of dissection	3D T1 VISTA	Occlusion
1	40s	Headache and transient motor weakness on the right side	Yes	Right VA	At 9 days of onset	No
2	50s	Neck pain and dizziness	No	Right VA	At 15 days of onset	No
3	40s	Transient motor weakness on the left side	Yes	Right ICA	At 12 days of onset	Yes
4	70s	Transient failure of vision and speech	No	Left ICA	At 13 days of onset	No
5	30s	Hemiplegia and Horner's syndrome	Yes	Right ICA	At 16 days of onset	Yes
6	30s	Neck pain and dizziness	Yes	Bilateral VAs	At 7 days of onset	Right (yes), left (no)
7	30s	Neck pain and hemiplegia	No	Left ICA	At 6 days of onset	Yes
8	30s	Neck pain and Horner's syndrome	Yes	Left ICA	At 15 days of onset	No
9	50s	Dizziness	Yes	Left VA	At 7 days of onset	Yes
10	30s	Aphasia and blurred vision	Yes	Left ICA	At 8 days of onset	No
11	40s	Neck pain and Brown-Séquard syndrome	Yes*	Right VA	At 6 days of onset	No
12	20s	Transient dizziness, double vision, and motor weakness on the right side	No	Bilateral VAs	At 11 days of onset	Right (yes), left (no)
13	30s	Headache and transient dizziness and motor weakness on the left side	No	Bilateral VAs	At 6 days of onset	No
14	20s	Dizziness and double vision	Yes	Left VA	At 3 days of onset	No
15	30s	Aphasia and hemiplegia	Yes	Left ICA	At 3 days of onset	Yes
16	50s	Asymptomatic	No	Left VA	NA	No
17	20s	Dizziness and hemiplegia	Yes	Left VA	At 22 and 56 days of onset	Yes
18	40s	Facial paralysis and aphasia	Yes	Bilateral VAs and bilateral ICAs	At 4 days of onset	No
19	70s	Dysarthria and hemiplegia	Yes	Left VA	At 3 days of onset	No
20	30s	Aphasia and hemiplegia	Yes	Left ICA	At 26 days of onset	Yes
21	40s	Dizziness, headache, and hemiplegia	Yes	Left VA	At 5 days and 23 days of onset	Yes

The diagnosis of dissection was not detected by T1 VISTA for patient number 20.
*Cervical spinal cord ischaemia was identified by MRI.
3D, three-dimensional; ICA, internal carotid artery; NA, not applicable; VA, vertebral artery; VISTA, volumetric isotropic turbo spin echo acquisition.

the possibility of dissection could not be excluded for six of them by VISTA (0/29 vs 6/17; p=0.001). For these six patients, the aetiology has not been determined for five of them (table 2), even after assessing all of the data, including T1 VISTA and DSA. 3D T1 VISTA showed hyperintense signals in the occluded artery segment without typical features of dissection. One of the patients was <30 years old without any risk factors of cerebrovascular diseases (patient number 25). The follow-up T1 VISTA for two of these five patients showed no recanalisation of the occluded arteries.

DISCUSSION

This study showed that the 3D T1 VISTA sequence at 3.0 T is useful in the diagnosis of spontaneous CAD. It can show intramural haematoma of the cervical artery clearly with a single acquisition and acceptable scan time. However, for some patients with totally acute occlusion of the artery without typical crescent-shaped hyperintense signals, a diagnosis of the aetiology of artery occlusion may be difficult by VISTA alone.

Several studies have investigated the efficiency of 3D black blood T1 sequences using variable refocusing

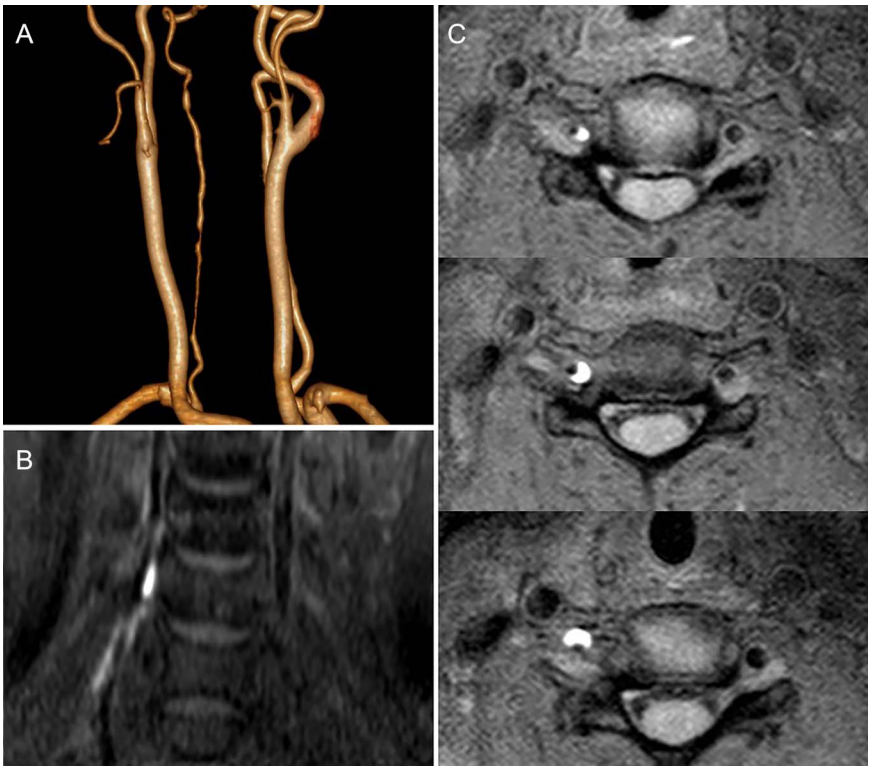

Figure 1 Patient number 1 with right vertebral artery dissection. (A) CT angiography shows stenosis of the right vertebral artery. (B) Curved planar reconstruction of three-dimensional (3D) T1 volumetric isotropic turbo spin echo acquisition (VISTA) images shows the arterial wall hyperintensity of the right vertebral artery. (C) Axial reconstructions of 3D T1 VISTA images show the crescent-like hyperintensity of the wall haematoma.

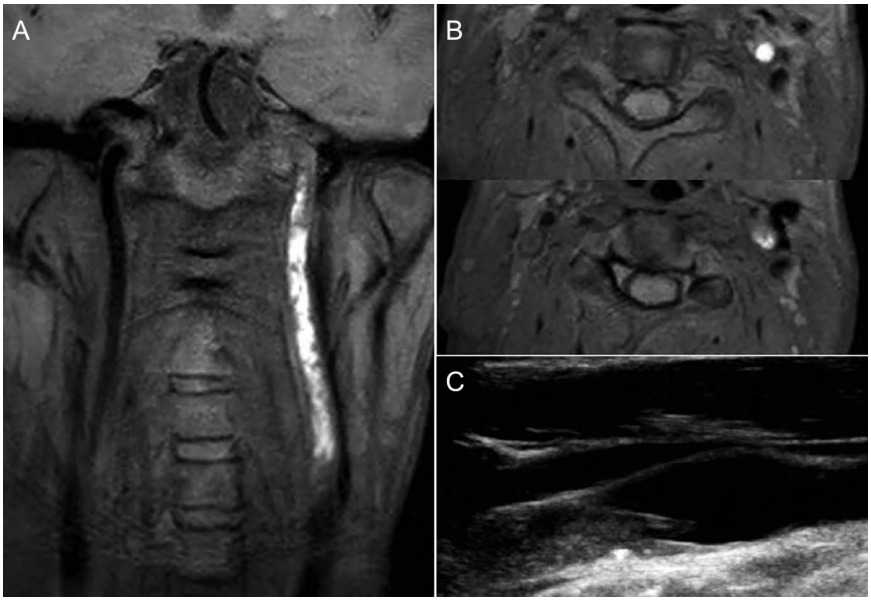

Figure 2 Patient number 20 with a left internal carotid artery dissection. (A) Coronal of three-dimensional (3D) T1 volumetric isotropic turbo spin echo acquisition (VISTA) image shows hyperintensity of the left internal carotid artery at 26 days of onset. (B) Axial reconstructions of 3D T1 VISTA images show the occluded left internal carotid artery without typical crescent-like hyperintensity. (C) Ultrasound of the left internal carotid artery at 15 days of onset shows a double lumen and intima.

flip-angle turbo-spin-echo imaging in the diagnosis of CAD. All of them showed that a 3D black blood T1 sequence is more useful than conventional imaging tools. Takemoto *et al*[17] first reported the value of T1 VISTA sequence at 1.5 T in the diagnosis of CAD. They concluded that a 3D black blood T1 sequence can improve the assessment of intramural haematoma in vertebral artery dissection compared with 2D spin-echo T1-weighted images and time-of-flight MRA (TOF-MRA).[16] Another study showed that abnormal vessel enhancement was recognised in 15 of 15 patients with vertebral artery dissection on contrast-enhanced T1 VISTA images. There are two other similar 3D black blood T1sequences that are commercially available (T1 CUBE and T1 SPACE from GE Healthcare, Milwaukee, Wisconsin and Siemens, Erlangen, Germany, respectively).[11 20] Studies showed that these two 3D black blood T1 sequences at 1.5 T or 3.0 T may also be a substitute

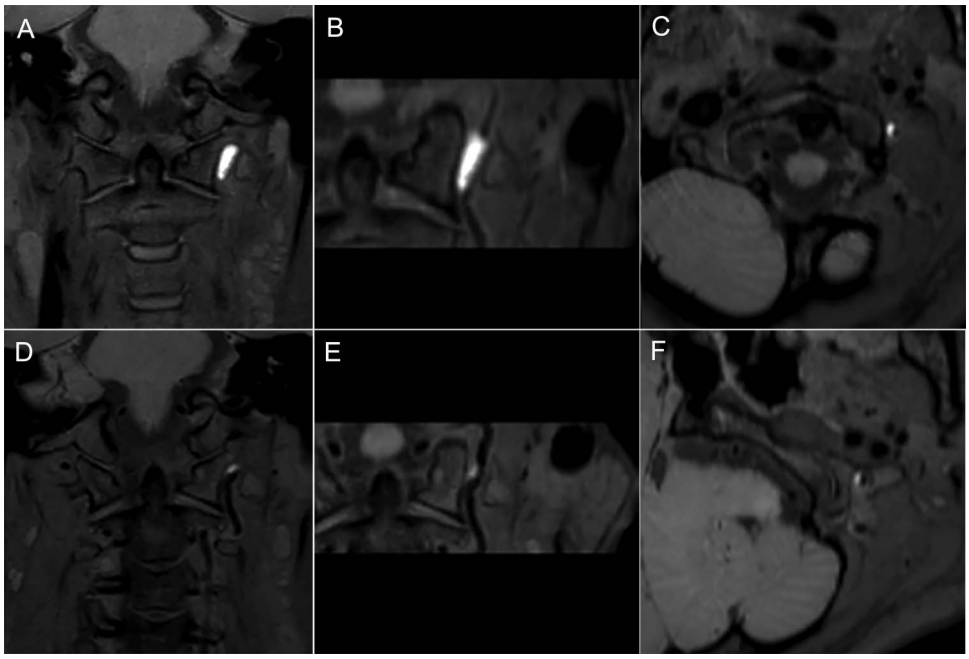

Figure 3 Patient number 21 with a left vertebral artery dissection. (A–C) Coronal of three-dimensional (3D) T1 volumetric isotropic turbo spin echo acquisition (VISTA) image, curved planar reconstruction of 3D T1 VISTA images and short-axis view of the left vertebral artery at 5 days of onset show high-signal intensity of the left vertebral artery. (D–F) A repeat scan at 23 days of onset shows the recanalisation of the occlusion and the residual intramural haematoma.

Table 2 Characteristics of patients without a definitive diagnosis of with or without dissection

Patient	Age	Symptoms	Acute infarction	Location of lesion	3D T1 VISTA	Occlusion
22	40s	Dizziness and hemiplegia	Yes	Bilateral VAs	At 18 days of onset	Yes
23	50s	Hemiplegia	Yes	Left ICA	At 25 and 48 days of onset	Yes
24	60s	Dizziness and double vision	Yes	Right VA	At 9 days of onset	Yes
25	20s	Dizziness and hemiplegia	Yes	Left VA	At 19 days of onset	Yes
26	60s	Hemiplegia	Yes	Right VA	At 15 days of onset	Yes

3D, three-dimensional; ICA, internal carotid artery; VA, vertebral artery; VISTA, volumetric isotropic turbo spin echo acquisition.

for 2D T1 sequences in the diagnosis of CAD.[11 20] The inter-rater and intrarater agreements were good for 3D black blood T1 sequences.[11 14]

There are several advantages of 3D black blood T1 sequences in the diagnosis of CAD compared with traditional imaging tools. First, this method can reveal the vessel wall of intracranial and extracranial arteries in a single acquisition with good image quality, good dark blood contrast, isotropic voxels, and a relatively short scan time. Second, the method can show the mural haematoma as high-signal intensity clearly. The mural haematoma is not easily identified from the source image of MRA and CTA and cannot be revealed by vascular images such as MRA, CTA, and DSA. Third, because of its isotropic volume acquisition, it can obtain the images of multiplanar reformation. Multiplanar reformation images can show the features of dissection at different angles and planes, which is especially helpful for an artery with tortuous course.

A recently published study showed that 3D simultaneous non-contrast angiography and intraplaque haemorrhage (SNAP) imaging can provide non-contrast MRA and vessel wall images simultaneously in a single acquisition with a shorter scanning time.[21] This study demonstrated excellent agreement with multisequence MRI in evaluating luminal stenosis and intramural haematoma in patients with craniocervical artery dissection. It seems that a 3D SNAP sequence may be a better choice than the aforementioned 3D black blood sequences because it can provide MRA and vessel wall images simultaneously in a single scan. However, this technique has not been widely investigated and is not commercially available.

We also investigated the limitations of 3D T1 VISTA in the diagnosis of CAD by analysing the patients for whom

a definite conclusion was not reached, with or without dissection by VISTA. Disagreement between the two readers for T1 VISTA existed for two patients who had acute artery occlusion. For one patient, the diagnosis of dissection was made by comprehensive analysis of ultrasound scan, T1 VISTA, and the other information. For the other patient, the diagnosis of dissection was made after a second scan with T1 VISTA. For five patients with acute artery occlusion, the aetiology has not been determined even after assessing all of the data including VISTA and DSA. All of this suggested that, for some patients with acute artery occlusion in whom even the aetiology may be dissection, the diagnosis of dissection cannot be made by T1 VISTA if there was no typical imaging features of dissection.

In this study, patients without artery occlusion all had a definite conclusion with or without dissection. However, for patients with artery occlusion, the possibility of dissection may not be excluded, especially for patients with occlusion of the vertebral artery because of its smaller size.[22] This suggested that the difference between intramural haematoma and intraluminal thrombus may be difficult with 3D T1 VISTA even at 3.0 T for some patients. For this group of patients, a follow-up scan, a contrast-enhanced scan, or an optimal VISTA technique may be helpful (patient number 16).[20]

There were several limitations in this study. First, the sample size was small and the contrast-enhanced imaging was not performed. Contrast-enhanced 3D T1 VISTA might be useful in manifesting subtle structure abnormalities, assessing vessel inflammatory reaction, and distinguishing intramural haematoma from intraluminal thrombus. Second, because previous studies already showed that a 3D black blood sequence can provide similar information and may be a substitute for 2D sequence, the 2D T1 black blood sequence was not performed for the patients. Third, we did not perform a follow-up 3D T1 VISTA scan for certain patients. Finally, all of the information including T1 VISTA were used to make the reference standard, which may lead to inaccurate results of the sensitivity and specificity for T1 VISTA.

CONCLUSIONS

In conclusion, this study showed that a 3D T1 VISTA sequence at 3.0 T is useful in the diagnosis of spontaneous CAD. This sequence can show intramural haematoma of the cervical artery clearly with a single acquisition and acceptable scan time. However, for some patients with totally acute occlusion of the artery without typical features of dissection, the unequivocal distinction between intramural haematoma and intraluminal thrombus may still be difficult with T1 VISTA alone. Future studies should investigate whether a repeat scan or an optimal VISTA technique would be useful for making a definite diagnosis.

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Contributors P-PN and YY contributed to the conception and design of the study, analysis and interpretation of the data, and drafting of the manuscript. P-PN performed the statistical analysis. H-WZ and YL contributed to the analysis of data and drafting of the manuscript. YL, Z-NG and HJ contributed to the design of the study, the acquisition of data, and drafting of the manuscript. All the authors approved the publication of the study.

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REFERENCES

1. Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. *Lancet Neurol* 2009;8:668–78.
2. Rahme RJ, Aoun SG, McClendon J Jr, *et al*. Spontaneous cervical and cerebral arterial dissections: diagnosis and management. *Neuroimaging Clin N Am* 2013;23:661–71.
3. Molina CA, Alvarez-Sabín J, Schonewille W, *et al*. Cerebral microembolism in acute spontaneous internal carotid artery dissection. *Neurology* 2000;55:1738–40.
4. Wang Y, Wang D. Hand in hand with the world to conquer stroke. *Stroke Vasc Neurol* 2016;1:1–2.
5. Caplan LR, Fisher M. Personalised care of patients with stroke in China: a challenge and an opportunity. *Stroke Vasc Neurol* 2016;1:3–5.
6. Mohan IV. Current optimal assessment and management of carotid and vertebral spontaneous and traumatic dissection. *Angiology* 2014;65:274–83.
7. Kim TW, Choi HS, Koo J, *et al*. Intramural hematoma detection by susceptibility-weighted imaging in intracranial vertebral artery dissection. *Cerebrovasc Dis* 2013;36:292–8.
8. Naggara O, Louillet F, Touzé E, *et al*. Added value of high-resolution MR imaging in the diagnosis of vertebral artery dissection. *AJNR Am J Neuroradiol* 2010;31:1707–12.
9. Blum CA, Yaghi S. Cervical artery dissection: a review of the epidemiology, pathophysiology, treatment, and outcome. *Arch Neurosci* 2015;2:pii: e26670.
10. Chen H, Li Z, Luo B, *et al*. Anterior cerebral artery dissection diagnosed using high-resolution MRI. *Neurology* 2015;85:481.
11. Cuvinciuc V, Viallon M, Momjian-Mayor I, *et al*. 3D fat-saturated T1 SPACE sequence for the diagnosis of cervical artery dissection. *Neuroradiology* 2013;55:595–602.
12. Bisseret D, Khalil A, Favrole P, *et al*. Spontaneous cervical artery dissection: role of a SE-T1-weighted fat-sat volume acquisition. *Diagn Interv Imaging* 2014;95:443–6.
13. Zhou Z, Li R, Zhao X, *et al*. Evaluation of 3D multi-contrast joint intra- and extracranial vessel wall cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2015;17:41.
14. Natori T, Sasaki M, Miyoshi M, *et al*. Detection of vessel wall lesions in spontaneous symptomatic vertebrobasilar artery dissection using T1-weighted 3-dimensional imaging. *J Stroke Cerebrovasc Dis* 2014;23:2419–24.
15. Sakurai K, Miura T, Sagisaka T, *et al*. Evaluation of luminal and vessel wall abnormalities in subacute and other stages of intracranial vertebrobasilar artery dissections using the volume isotropic turbo-spin-echo acquisition (VISTA) sequence: a preliminary study. *J Neuroradiol* 2013;40:19–28.
16. Takano K, Yamashita S, Takemoto K, *et al*. MRI of intracranial vertebral artery dissection: evaluation of intramural haematoma using a black blood, variable-flip-angle 3D turbo spin-echo sequence. *Neuroradiology* 2013;55:845–51.
17. Takemoto K, Takano K, Abe H, *et al*. The new MRI modalities "BPAS and VISTA" for the diagnosis of VA dissection. *Acta Neurochir Suppl* 2011;112:59–65.

18. Bossuyt PM, Reitsma JB, Bruns DE, *et al*. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *BMJ* 2015;351:h5527.
19. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
20. Edjlali M, Roca P, Rabrait C, *et al*. 3D fast spin-echo T1 black-blood imaging for the diagnosis of cervical artery dissection. *AJNR Am J Neuroradiol* 2013;34:E103–6.
21. Li Q, Wang J, Chen H, *et al*. Characterization of craniocervical artery dissection by simultaneous MR noncontrast angiography and intraplaque hemorrhage imaging at 3T. *AJNR Am J Neuroradiol* 2015;36:1769–75.
22. Markus HS, Hayter E, Levi C, *et al*., CADISS trial investigators. Antiplatelet treatment compared with anticoagulation treatment for cervical artery dissection (CADISS): a randomised trial. *Lancet Neurol* 2015;14:361–7.