Clinical Neurology and Neurosurgery 137 (2015) 105–111

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

A novel application of four-dimensional magnetic resonance angiography using an arterial spin labeling technique for noninvasive diagnosis of Moyamoya disease☆

Haruto Uchino[a], Masaki Ito[a,*], Noriyuki Fujima[b], Ken Kazumata[a], Kazuyoshi Yamazaki[a], Naoki Nakayama[a], Satoshi Kuroda[c], Kiyohiro Houkin[a]

[a] Department of Neurosurgery, Hokkaido University Graduate School of Medicine, N15 W7, Kita-ku, Sapporo 060-8638, Japan
[b] Department of Radiology, Hokkaido University Graduate School of Medicine, N15 W7, Kita-ku, Sapporo 060-8638, Japan
[c] Department of Neurosurgery, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama 930-0914, Japan

ARTICLE INFO

Article history:
Received 31 October 2014
Received in revised form 14 June 2015
Accepted 5 July 2015
Available online 7 July 2015

Keywords:
Arterial spin labeling
Cerebrovascular
Four-dimensional magnetic resonance angiography
Moyamoya disease
Postoperative hyperperfusion

ABSTRACT

Background: Noncontrast-enhanced time-resolved four-dimensional magnetic resonance angiography using an arterial spin labeling technique (ASL-4D MRA) is emerging as a next generation angiography for the management of neurovascular diseases. This study evaluated the feasibility of ASL-4D MRA for the diagnosis of Moyamoya disease (MMD) and MMD staging by using digital subtraction angiography (DSA) and time-of-flight MRA (TOF MRA) as current standards.
Methods: Eleven consecutive non-operated patients who underwent DSA for the diagnosis of MMD were recruited. Two independent observers evaluated the three tests. The data were analyzed for inter-observer and inter-modality agreements on MMD stage. Nine of 22 hemispheres underwent surgical revascularization and ASL-4D MRA was repeated postoperatively.
Results: Time-resolved inflow of blood through the cerebral vessels, including moyamoya vessels, was visualized in all the 22 non-operated hemispheres. MMD stages assessed by DSA and ASL-4D MRA were completely matched in 18 hemispheres, with a significant positive correlation between these modalities ($r = 0.93$, $P < 0.001$). Inter-observer agreement with ASL-4D MRA ($\kappa = 0.91 \pm 0.04$, $P < 0.001$) and inter-modality agreement between ASL-4D MRA and DSA ($\kappa = 0.93 \pm 0.04$, $P < 0.001$) were both excellent. MMD stages assessed by ASL-4D MRA have also a significant positive correlation with those assessed by TOF MRA ($r = 0.68$, $P = 0.004$). Repeated ASL-4D MRA clearly demonstrated the bypassed arteries and changes in the dynamic flow patterns of cerebral arteries in all the nine hemispheres after surgical revascularization. Of these, postoperative focal hyperperfusion was detected by single photon emission tomography in 7 hemispheres. In five of the seven hemispheres (71%) with postoperative hyperperfusion, ASL-4D MRA demonstrated focal hyperintense signals in the bypassed arteries, although TOF MRA did not.
Conclusions: Noninvasive ASL-4D MRA is feasible for the diagnosis of MMD staging. This next generation angiography may be useful for monitoring disease evolution and treatment response in cerebral arteries after revascularization surgery in MMD.

1. Introduction

Moyamoya disease (MMD) is an idiopathic cerebrovascular disease characterized by chronic progressive stenosis of the terminal portion of the bilateral internal carotid arteries (ICAs) around the circle of Willis, which leads to the formation of collateral vascular networks that look like "a puff of smoke" (moyamoya vessels) at the base of the brain [14]. Although digital subtraction angiography (DSA) has been recommended for a definitive diagnosis of MMD and MMD staging (known as a 6-grade Suzuki's stage system), especially in candidates of surgical revascularization [12], this procedure is known to carry a potential risk of persistent neurological deficits [1]. When certain findings are fulfilled on time-of-flight (TOF) imaging conducted using a ≥1.5-Tesla scanner, magnetic resonance angiography (MRA) can also provide a definitive diagnosis

☆ This work has been presented in part at the 3rd international Moyamoya meeting in August 2013, in Sapporo Japan.

* Corresponding author. Present address: Department of Neurosurgery, Stanford University School of Medicine, 1201 Welch Road, MSLS P320, Stanford, CA 94305-5487, USA.
E-mail address: masakiitou-nsu@umin.ac.jp (M. Ito).

http://dx.doi.org/10.1016/j.clineuro.2015.07.003
0303-8467/

[12]. However, TOF MRA does not have temporal resolution. It would be ideal if dynamic flow patterns within the cerebral vasculature were demonstrated noninvasively to monitor clinical course of MMD. Growing evidence revealed that a 3.0-Tesla MR scanner offers a higher signal-to-noise ratio, allowing a higher spatial resolution and a refined visualization of features of intracranial neural and vascular structures, including pathological vasculature in patients with MMD [9,13]. Recently, noncontrast-enhanced time-resolved four-dimensional MRA using an arterial spin labeling technique (ASL-4D MRA) was developed to delineate dynamic flow patterns within the cerebral vasculature [18]. Although conventional contrast agent-enhanced dynamic MRA with some temporal resolution has received considerable attention [11], this imaging technique still has limitations, including requirements of intravenous contrast agent injection as well as the low temporal resolution (only on the order of seconds) [18]. ASL-4D MRA can be performed without any contrast agent by labeling circulating protons in arterial blood of the targeted vessels. The dynamic inflow pattern of arteries, including intracranial ones, can be visualized with higher temporal resolution (on the order of milliseconds) [17]. Growing number of studies has already tested ASL technique to measure cerebral perfusion parameters, including cerebral blood flow and arterial transit time in various type of central nervous system pathology, including MMD [16]. On the other hand, this novel technique has been tested as a time-resolved cerebral angiography only for cerebral arteriovenous malformations [17]. Thus, it has not been tested in patients with MMD. In the present study, therefore, the feasibility of ASL-4D MRA was evaluated for the diagnosis of MMD and MMD staging by using DSA and TOF MRA as current standards. In patients who underwent surgical revascularization, ASL-4D MRA was further repeated after surgery and the changes in the dynamic flow patterns within the cerebral vasculature were tested.

2. Materials and methods

2.1. Study subjects

This prospective study included 11 consecutive patients with MMD who were treated at the Hokkaido University Hospital between June 2012 and February 2013. They all met the criteria for definitive MMD as determined by the Suzuki's stage classification based on the DSA findings [14]. MRI examinations, including ASL-4D MRA and TOF MRA, were performed on all the patients before surgery. The MRA stage was also assigned for all the 22 hemispheres in 11 patients according to the individual TOF MRA total score described elsewhere [5]. The mean period between DSA and ASL-4D MRA examination was 4.5 months (range: 0–13). In 7 cases with a period longer than 1 month between DSA and ASL-4D MRA, we confirmed that the TOF MRA stage did not progressed. All the 11 patients cover all six types of clinical events or symptoms of MMD reported previously: [12] cerebral infarction, transient ischemic attack, intracerebral hemorrhage, headache, epilepsy, and asymptomatic.

2.2. Protocol for ASL-4D MRA

All MR scanning were performed using a 3.0-Tesla scanner (Achieva 3T TX Release 3.2.1.0; Philips Medical Systems, Bests, Netherlands) with a 32-channel head coil. The Pulsed ASL was performed using echo planar imaging and signal targeting with alternating radiofrequency (EPI-STAR) technique [2]. Labeling was achieved by applying section-selective 180° radiofrequency pulses in a 30.0-mm-thick labeling slab that was located below the imaging plane. Image acquisition was performed using Look-Locker sampling with an excitation pulse of 10° [7], and various delay times; post-labeled delay of 200 ms after labeling and a subsequent constant phase interval of 150 ms were used. Imaging plane was located sufficiently to cover the circle of Willis and the associated main branches in all the patients. As a result, a total of eight phases were acquired (200, 350, 500, 650, 800, 950, 1100, and 1250 ms after labeling). A turbo-field echo-planar imaging (TFEPI) sequence was used as readout. Other imaging parameters were set as follows to adjust scanning time to approximately 5 min: TR, 13 ms; TE, 5.1 ms; cycle duration, 1460 ms; FOV, 230 mm × 230 mm; slab thickness, 105 mm; matrix, 192 × 192; slice thickness, 0.7 mm; voxel size, 1.2 mm × 1.2 mm × 0.7 mm; turbo field echo (TFE) factor, 13; EPI factor, 5; sensitivity encoding (SENSE) factor, 3; and Flip angle, 10°. After ASL-4D MRA was completed, a routine MRI scan, including TOF MRA was performed as part of the routine diagnostic protocol, which was reported elesewhere [5].

Table 1
Protocol for imaging evaluation to determine the Suzuki's stage by ASL-4D MRA.

Suzuki's stage	Angiographic findings
Stage I	Narrowing of the carotid fork
Stage II	Dilated major cerebral artery and a slight moyamoya vessel network
Stage III	Discontinuity of the proximal portion of ACA and/or MCA with distinct basal moyamoya vessels
Stage IV	Disappearance of ACA and/or MCA and/or PCA and narrowing of basal moyamoya vessels
Stage V	Disappearance of all the main cerebral arteries arising from the ICA system without basal moyamoya vessels
Stage VI	Complete disappearance of the intracranial ICA and main cerebral arteries arising from the ICA system without basal moyamoya vessels

2.3. Determination of Suzuki's disease stage by ASL-4D MRA

ASL-4D MRA was performed on all the non-operated 11 patients prior to surgical revascularization, within an average of 4.4 months (range: 0–13 months) after the most recent DSA exam. Two authors (HU and MI) who are expertized at radiological diagnosis for Moyamoya disease and also are certificated as board neurosurgeons by Japan Neurosurgical Society (more than 7- and 11-years experience, respectively) used ASL-4D MRA data to independently diagnose the MMD stage of each patient (22 hemispheres). A board diagnostic-neuro-radiologist of Japan Radiological Society (third author, NF) confirmed these two raters to be satisfied for intra-rater agreement indices of the staging of Moyamoya disease. Based on Suzuki's stage classification, cerebral angiography on ASL-4D MRA were analyzed bilaterally for stenosis, occlusion of the terminal portion of ICA or the proximal portions of the anterior, middle and/or posterior cerebral artery (ACA, MCA and/or PCA), as well as for the development of basal moyamoya vessels [12,14]. In brief, each six-grade stage was assigned when ASL-4D MRA demonstrated each of findings as described in Table 1. First, we compared inter-observer differences in the diagnosis of Suzuki's stage classification determined by time-resolved ASL-4D MRA. Next, inter-observer disagreements on the stage determined by ASL-4D MRA were resolved during a consensus meeting with all the co-authors, including abovementioned board diagnostic-neuro-radiologist of the present study. Third, the inter-modality differences in the diagnosis of the stage between time-resolved modalities (i.e.; DSA and ASL-4D MRA) were also compared. In addition, six-grade-Suzuki's stage determined by ASL-4D MRA was compared to four-grade-MRA stage determined by TOF MRA, however, it was impossible to calculate kappa coefficient for the inter-modality agreement between these modalities due to the difference of the number of grades. Finally, the sensitivity, specificity, true/false predictive value, and accuracy of the diagnosis were calculated for each Suzuki's stage classification.