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Chronic intracranial artery stenosis: Comparison of whole-brain arterial spin labeling with CT perfusion

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ABSTRACT

Purpose: To evaluate the potential clinical value of Arterial spin-labeled (ASL) through comparison with computed tomography perfusion (CTP) in patients with chronic intracranial artery (middle cerebral artery, MCA) stenosis.

Methods: Twenty-nine patients (14 female, average ages 62) were included in our study from October 2013 to August 2016. Relative cerebral blood flow (rCBF) in the MCA territory was calculated on both ASL and CTP. Patients were divided into three groups (mild, moderate and severe) based on their degree of MCA stenosis on DSA. The paired *t*-tests and Bland-Altman plots were used to evaluate the differences of rCBF between ASL and CTP.

Results: There was a significant difference in rCBF between ASL and CTP for all patients ($P < 0.001$) and for those with severe MCA stenosis ($P < 0.001$). For patients with mild or moderate stenosis, there were no significant differences ($P = 0.496$ and 0.645, respectively). The 95% limits of agreement for all patients and those with severe stenosis were (−0.25, 0.41) and (−0.13, 0.56), respectively. For patients with mild or moderate stenosis, the values were (−0.21, 0.22) and (−0.20, 0.19).

Conclusion: Compared with CTP, ASL tended to overestimate the perfusion deficit in patients with severe chronic MCA stenosis. However, ASL is noninvasive, repeatable method and can be a promising clinical diagnostic tool to evaluate patients with intracranial stenosis.

1. Introduction

Arterial spin labeling (ASL) is a noninvasive magnetic resonance perfusion imaging technique that uses magnetically labeled arterial bold water as endogenous diffusible tracer. The labeled images is subtracted from the pre-labeling condition and is a relative measure of local perfusion, and suitable for repeated measurements [1]. It was first proposed in the early 1990s. Recent advances in magnetic resonance imaging (MRI) technology, including stronger magnetic fields, array receiver coils, pseudo continuous ASL and rapid three-dimensional (3D) acquisition techniques have markedly improved the signal to noise ratio of ASL, which has resulted in its increased use in clinical neuroimaging [2]. Preliminary studies have shown that ASL can detect both hypo- and hyperperfusion as well as delayed transit effects that may differentiate clinical outcomes in acute ischemic stroke [3].

CT perfusion(CTP) has been relatively widely used in clinical practice for brain perfusion measurement. Due to the linear relationship between contrast concentration and attenuation, CTP can provide relatively accurate perfusion quantitative parameters [4]. However the disadvantage of CTP includes the radiation dose and contrast media injection. While ASL would be ideal and important for assessments of hemodynamics in patients with intracranial stenosis. The aim of our study was to evaluate the potential clinical value of ASL in detecting cerebral blood flow (CBF) changes in chronic ischemic stroke by comparing with CTP as a reference standard.

Abbreviation: ASL, arterial spin-labeled; CTP, computed tomography perfusion; MCA, middle cerebral artery; rCBF, relative cerebral blood flow; MRI, magnetic resonance imaging; DSA, digital subtraction angiography; pcASL, pulsed continuous ASL; ATT, arterial transit time; TL, labeling time; PLD, post-labeling delay

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2. Materials and methods

2.1. Patients

Institutional review board approval was obtained for this retrospective study, and written informed consent was obtained from all patients. Between October 2013 and August 2016, 110 patients underwent CTP, ASL and digital subtraction angiography (DSA) examination in our hospital. To evaluate the potential clinical value of ASL through comparison with CTP in detecting cerebral blood flow (CBF) changes in chronic ischemic stroke, patients were included in this study if they met the following criteria: (1) only unilateral MCA stenosis or occlusion was present, confirmed by DSA, with no stenosis of any other cerebral artery; (2) symptoms due to transient ischemic attacks or ischemic stroke related to MCA stenosis had been present and lasting more than a month; and (3) CTP and ASL were conducted within 2 days of each other and during that interval the patient did not undergo any treatment. The exclusion criteria were: (1) patients with a history of contrast medium allergy or renal failure; (2) patients with general contraindications to MRI examination; (3) the symptoms had increased gradually or new symptoms appeared within the preceding 1 week; (4) stenosis of another cranial or carotid artery was present; (5) intracranial hemorrhage was observed on CT; and (6) stroke was caused by cardiogenic embolism, hypotension, coagulopathy or other systemic disease (e.g. moyamoya disease).

2.2. ASL protocol

All patients underwent MRI on a 3 T clinical scanner (HD.xt Twin Speed; GE Medical Systems, Milwaukee, WI, USA) using an eight channel receive-only head coil for signal reception. The scans employed our institution's standard protocol for patients with brain disease, comprising axial T2 weighted, axial T1 weighted and coronal fluid attenuated inversion recovery sequences, axial 3D time of flight angiography, axial diffusion weighted imaging and ASL. ASL was performed with a background suppressed, pulsed continuous ASL (pCASL) sequence, using a 3D stack of spirals fast spin echo readout [5,6]. Thirty-two axial slices were collected with repetition time = 5500 ms, echo time = 25 ms, slice thickness = 5 mm, field of view = 24 cm and matrix = 128 × 128. The labeling time (TL) was 1800 ms and a post-labeling delay (PLD) of 2000 ms was used to reduce errors from transit time effects [7]. Vascular crushing gradients were not applied. Images were analyzed on a commercially available dedicated workstation (Advantage, software version 4.3; GE Medical Systems). CBF maps were generated from ASL data [8,9].

2.3. CTP protocol

CT images were acquired on a multi detector row CT system (Aquilion ONE; Toshiba Medical Systems, Tokyo, Japan) with a detector width of 16 cm and 320 detector rows (640 slices). Nineteen whole-head volumes were acquired after bolus injection of 50 mL of iodinated contrast agent (Iopamidol; Bracco Sine Pharmaceuticals, Shanghai, China) at a rate of 5 mL/s, and then 20 mL of physiological saline (0.9%) was injected at 4–5 mL/s. The CTP protocol was started 7 s after contrast fluid injection, with a high-dose volumetric scan at 310 mA, followed after 4 s by 3 scans at 150 mA, 6 scans at 300 mA, 4 scans at 150 mA, one every 2 s, at 100 mA, then by 5 scans, one every 5 s. The overall scan time was 60 s. Whole-brain CTP images were reconstructed on a Vitrea workstation (fX ver6.0; Vital Images, Minnetonka, MN, USA) in accordance with the 19 whole-head volumes. CBF perfusion parameters were calculated from time–density curves.

2.4. Image analysis

The slice thickness for both ASL and CTP imaging was 5 mm. Regions of interest (ROIs) in the cerebral cortex of MCA territory on CTP images were drawn automatically by the analysis software; ROIs on ASL images were drawn manually on the same areas as for CTP by two neuroradiologists who were unaware of the degree of stenosis or clinical history. CBF in the MCA distribution of the whole brain was recorded. In each patient, the MCA ROI from each of 10 slices were used, producing 10 ipsilateral and 10 contralateral ROIs per CTP or ASL examination, per patient. Relative CBF (rCBF) was calculated as the ratio of CBF measured on the side of the lesion to that of the homologous region on the contralateral hemisphere.

DSA was performed within 1 week of CTP and ASL. On DSA, the diameter of the artery was measured according to the Warfarin-Aspirin Symptomatic Intracranial Disease method and the percentage stenosis was calculated as [1-(stenosed diameter/normal diameter)] × 100 [10]. The patients were divided into three groups according to their degree of stenosis, which was classified as mild (< 50%), moderate (50–69%) or severe (≥70%). Diameter measurements were made by a blinded image reader with 6 years' experience independently and verified by another experienced neuroradiologist with 25 years' experience.

2.5. Statistical analysis

The inter-reader agreement of two readers for ROIs drawing on ASL images and artery diameter measurement were calculated.

The paired *t*-test was employed to assess the significance of differences in rCBF between CTP and ASL, using PASW Statistics ver18.0 (IBM, Armonk, NY, USA), and to compare rCBF between CTP and ASL for each stenosis subgroup. $P < 0.05$ was considered significant. Bland-Altman plots were used to evaluate the rCBF value agreement between ASL and CTP [11], using MedCalc ver14.10.2 (MedCalc Software, Mariakerke, Belgium).

3. Results

Indeed, 29 patients (14 female, 15 male) who met our inclusion and exclusion criteria were included in this study. The average age was 62 years (range 28–84 years). Fifty five patients were excluded due to the presence of multiple intracranial artery stenosis or occlusion on DSA, while another 38 patients were excluded because of lack of DSA, CTP or ASL examination. Seven patients with new symptoms appeared within the preceding 1 week and 10 patients with intracranial hemorrhage were also excluded. Twenty nine patients met more than one exclusion criteria.

All 29 patients presented with clinical symptoms lasting more than a month. Nine patients presented difficulty with speaking, 8 patients with dizziness, and 12 patients with limb weakness. The baseline clinical data for all the patients was shown in Table 1.

The interval between ASL and CTP was 6 h for 9 patients, 1 day for 12 patients and 2 days for 8 patients. The inter-reader agreement of two readers for ROIs drawing on ASL images and artery diameter measurement were both good, with a kappa statistic of 0.981 (0.972, 0.988) and 0.905 (0.870, 0.931). All patients showed evidence of unilateral MCA stenosis or occlusion on DSA. According to DSA, 9 patients were mild MCA stenosis, 9 were moderate and 11 were severe. The results of paired *t*-tests comparing CTP and ASL are shown in Table 2. There was a significant difference in rCBF between ASL and CTP for all the 29 patients ($t = 8.186$, $P < 0.001$). There was significant difference between CTP and ASL for patients with severe MCA stenosis ($t = 12.694$, $P < 0.001$). While there was no significant difference between two methods for patients with mild ($t = 0.684$, $P = 0.496$) or moderate ($t = -0.462$, $P = 0.645$) stenosis.

The data for Bland-Altman plots are illustrated in Fig. 1. The mean absolute difference (bias) in rCBF between CTP and ASL and the 95% confidence interval of the mean difference (limits of agreement) were 0.08 (0.06, 0.10) for all the patients and 0.01 (−0.02, 0.03), 0.00