学 位 論 文 の 要 旨

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学　位　論　文　名　Distinctive Patterns of Three-Dimensional Arterial Spin-Labeled Perfusion Magnetic Resonance Imaging in Subtypes of Acute Ischemic Stroke

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論 文 内 容 の 要 旨

INTRODUCTION

Arterial spin-labeling (ASL) is a noninvasive magnetic resonance imaging (MRI) technique used to assess quantitatively brain perfusion in humans. ASL-MRI is associated with minimal risk and expense compared to imaging methods using exogenous tracers. It has been applied to elucidate the mechanism underlying ischemic penumbra, defined as a perfusion-diffusion mismatch in patients with acute ischemic stroke (AIS). However, few studies have investigated the clinical advantages of ASL in various types of AIS. We investigated the clinical utility of ASL for evaluating AIS and its medical treatment in a group of serially enrolled patients with AIS who were admitted within 24 h after onset.

MATERIALS AND METHODS

The 55 male and 48 female patients (mean age, 79.0 years) underwent diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery imaging, MR angiography, and pulsed continuous ASL perfusion imaging to determine stroke subtype and abnormality in ASL image. Arterial transit artifacts (ATA), indicative of occlusive regions or collateral flow, and other stroke indices were also compared. Neurological deficits were scored by the National Institute of Health Stroke Scale (NIHSS). Informed consent was provided by the patients and/or their families. The study protocol was approved by Ethics Committee of the Ohda Municipal Hospital.

Images were interpreted qualitatively in random order by two neurologists (N.K. and K.O.) blinded to the patients' data. DWI lesions were classified according to size as small (lesion diameter ≤ 1.5 cm), medium, and large (encompassing the entire distribution area of the major brain vessel). MRA abnormalities were defined as stenosis > 50% or occlusion of the major infarct-related brain vessel. ASL findings were classified according to hypoperfusion size as none (no abnormal findings), focal (hypo- or hyperperfusion less extensive than diffuse), and diffuse (hypo- or hyperperfusion encompassing the entire distribution area of the major brain vessel). The presence of perfusion deficits and diffusion-perfusion mismatches (DPM), defined as a perfusion/diffusion volume (PDV) ratio > 1.2 was also assessed. The presence of an arterial transit artifact (ATA), seen as a bright intraluminal area (10) on ASL images, was also determined.

Inter-observer agreement regarding ASL abnormality patterns was assessed using kappa (κ) statistics. A κ value > 0.6 was defined as good agreement, and κ > 0.8 as excellent agreement. The frequency of positive ASL findings in each stroke group was compared using the χ^2 test and the column proportion test followed by a Z test for post-hoc analysis. SPSS for Windows software (ver. 22; SPSS Inc., Chicago, IL, USA) was used for all analyses. Two-sided P-values < 0.05 were considered to indicate statistical significance.

RESULTS AND DISCUSSION

The average time between symptom onset and image acquisition was 4.7 h. Agreement between readers for DWI and ATA was perfect, and agreement regarding an ASL abnormality was excellent.

ASL hypoperfusion was detected in 3 of 9 patients with transient ischemic attack (TIA), 2 of 27 with lacunar infarction (LI), 19 of 31 with atherothrombotic infarction (AT), and 30 of 36 with cardiogenic embolic infarction (CE). The rate of ASL abnormalities, ATAs, the rate of a diffuse pattern and DPM positivity were significantly lower and the rate of no ASL abnormality was significantly higher in LI than in AT and CE. ASL abnormalities were more prevalent in patients with medium-to-large DWI-assessed lesions than in those with small lesions on DWI. Patients with medium-sized lesions following AT and CE had a high frequency of diffusion-perfusion mismatch.

Intravenous tissue plasminogen activator (t-PA) therapy was administered to 5 patients. The improvement of clinical symptoms was achieved in all 5 patients and their mean NIHSS score was 12 on admission and 1 at discharge. The mean NIHSS score of the patients who were not treated with t-PA was 8.5 on admission and 12.4 at discharge. The prognosis of patients who received t-PA therapy was significantly better than that of patients who did not. Except for 1 patient with a brainstem lesion, all of them showed hemodynamic improvement associated with

recanalization. An improvement in ASL-detected hypoperfusion in these 4 patients supports the usefulness of this technique as an imaging marker of clinical outcome.

The DWI patterns of the lesions varied from none to large. The frequency of normal ASL image was significantly higher in the group with small lesions than with medium- and large-sized lesions. Diffuse ASL abnormalities were detected significantly less often in patients with small-sized abnormality compared to medium- and large-sized abnormalities. The prevalence of DPM was significantly higher in patients with medium-sized lesions than in those with small-sized lesions. The frequency of MRA and ATA was significantly lower in patients with small-sized lesions than in those with medium- and large-sized lesions.

The combined ASL and ATA findings revealed a high abnormality rate (77.5%) in our AIS patients. The ASL patterns in our patients varied from no lesion to a diffuse pattern, depending on the stroke subtype. To the best of our knowledge, this is the first study to evaluate the relationship between ASL findings and stroke subtype combined with DWI-determined lesion size. The specific features may be explained by the distinct pathophysiological hemodynamic changes that occur in the various stroke subtypes. Thus, patients with LI, who in most cases had small lesions on DWI, had no ASL abnormalities, whereas in patients with AT and CE, who were more likely to have medium- to large-sized lesions, highly diffuse abnormalities were frequently detected. The prevalence of ATA associated with DPM was significantly higher in the AT and CE groups than in the LI group. DPM was most frequently observed in the patient group with medium-sized lesions. These findings may serve as a useful reference in decision-making related to acute stroke therapy.

In our study, the frequency of ATA and MRA was significantly low in LI and high in CE, which indicated that ATA reflects the hemodynamic pathology at the sites of perforating small vessel lesions or acute obstruction of a major arterial trunk. Conversely, the lack of ATA development following an AT type stroke can perhaps be attributed to the gradual progressive arterial obstruction in atherothrombotic cerebral infarction.

CONCLUSION

Our results demonstrate the utility of ASL in revealing the pathophysiology underlying the stroke-related hemodynamic state and in guiding decision-making for the optimal treatment of AIS patients depending on the stroke subtype.