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Vertebral artery hypoplasia, posterior circulation infarction and relative hypoperfusion detected by perfusion magnetic resonance imaging semiquantitatively

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ABSTRACT

Vertebral artery hypoplasia (VAH) has been considered a risk factor of posterior circulation infarction (PCI), especially in the territory of the posterior inferior cerebellar artery (PICA). But whether VAH is an independent risk factor for PCI remains uncertain and how VAH participates in the evolvement of PCI is still not clear either. Therefore, this study aims to examine whether VAH is an independent risk factor for PCI and evaluate the effect of VAH on the cerebral perfusion in the territory of the PICA detected by perfusion magnetic resonance imaging (MRI) semiquantitatively. Both univariate and multivariate analyses showed that VAH, hypertension and smoking were more frequent in patients with PCI than in patients without PCI. Perfusion MRI analysis found that there were remarkable differences in the frequency of the relative cerebral blood flow (rCBF) value ≤0.85 and the relative time to peak (rTTP) values between VAH patients without PCI and non-VAH patients without PCI. Our results indicated that VAH may be an independent risk factor for PCI, especially in the presence of hypertension and smoking and that a relative hypoperfusion associates with VAH that may contribute to the evolvement of the infarction in the PICA territory.

1. Introduction

Vertebral artery hypoplasia (VAH) is a relatively common congenital vascular variation and there is no standard definition in terms of VA diameter ranging from <2 mm to <3 mm or an asymmetry ratio ≥ 1:1.7 [1–3,6]. Previous studies observed that VAH was associated with posterior circulation infarction (PCI), especially in the territory of its branch posterior inferior cerebellar artery (PICA) and in coexistence with conventional risk factors for stroke [4–8]. But whether VAH is an independent risk factor for PCI remains uncertain and how VAH participates in the evolvement of PCI is still not clear either.

Studies have revealed that healthy subjects with VAH demonstrated electroneurophysiological abnormalities in the brainstem area [9], even among vertebral artery dominance (VAD) subjects [10]. Moreover, ultrasound studies have revealed that VAH may result in a decrease of the ipsilateral net VA blood flow volume [11]. Therefore, it has been assumed that a relative hypoperfusion caused by VAH might play an important role [10,12,13,15]. But few studies have been carried out to confirm it directly.

Dynamic perfusion computed tomography (CTP) and perfusion weighted magnetic resonance have been widely applied to evaluate brain hemodynamics in cerebrovascular diseases and could provide multiple parameters such as cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and time to peak (TTP), which can be interpreted visually or semiquantitatively [14]. A recent study concluded that VAH could lead to a relative regional hypoperfusion in the PICA territory with the method of evaluating the whole-brain CT perfusion (WB-CTP) visually [15]. However, the approach of visual assessment inevitably led to reader variation. So the aim of our investigation was to examine whether VAH is an independent risk factor for posterior circulation infarction (PCI) and relative hypoperfusion exists in corresponding territory by dynamic susceptibility contrast perfusion magnetic resonance imaging (DSC-PWI) semiquantitatively.

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2. Materials and methods

2.1. Subjects

Vertebral artery diameter was retrospectively determined in 187 consecutive patients who were admitted to the Department of Neurology from People's Hospital of Zhengzhou and underwent dynamic susceptibility contrast perfusion-weighted magnetic resonance imaging (DSC-PWI) within 5 days after the onset of symptoms because of suspect stroke from December 2014 to July 2015. Patients who did not undergo diffusion-weighted MR imaging(DWI) and apparent diffusion coefficient (ADC), contrast-enhanced magnetic resonance angiography (CE-MRA), or complicated with significant local stenosis (diameter > 50%) were excluded. Population admission baseline including age, gender, alcoholism (currently drinking or those who had stopped for <1 year), smoking (currently smokers or those who had stopped for <1 year), hypertension, diabetes, hyperlipidemia, coronary heart disease, weight, height, and National Institute of Health stroke scale (NIHSS) were recorded. The institutional ethics committee approved the study and every patient enrolled signed written informed consent form.

2.2. MR examination protocol and image processing

MRI examinations were performed in a GE Signa EXCITE 3.0T HDX (Fairfield, Connecticut, USA).

Cervical contrast enhanced magnetic resonance angiography (CE-MRA) was performed with a three-dimensional time-of-flight (3D-TOF) sequence with a TR of 4.8, TE of 1.6/Fr, field of view (Fov) of 320 × 320 mm, acquisition matrix 360 × 224 and slice thickness of 1.8 mm. Maximum intensity projection (MIP) were used to reconstruct images.

DWI was acquired using spin-echo echo planar imaging sequence (field of view 220 × 220 mm, acquisition matrix 160 × 160, TR5000, TE 77.6, slice thickness 5.0 mm).

Dynamic susceptibility contrast perfusion magnetic resonance imaging (DSC-PWI) was obtained with the scan parameters of TR (1500 ms), TE (15.2 ms), field of view (24 mm × 24 mm), acquisition matrix (130 × 128), slice thickness/space between the slices (5.0/1.5 mm) using a gradient-echo echo planar imaging sequences. A large-bore 18-gauge intravenous cannula was inserted to administer a 0.2 ml/kg bolus of gadopentetate dimeglumine (Gd-DTPA) at a rate of 4 ml/s, followed by an equal dose of saline immediately. 24 slices for whole brain coverage, and 50 consecutive times were repeated to obtain MR signal and a total of 1200 (24 × 50) raw images were generated.

2.3. Analysis of VA diameter Using CE-MRA

All raw scanning images were processed by the software AW Volume Share 5 (Volume View, version 9.4.05). Three dimensional maximum intensity projection (3D-MIP) reconstructed images were obtained and the diameter of the whole VAs was measured in the multiplanarly reformed window with the same settings for all enrolled patients. Diameter of all 4 segments (V1–V4) was measured. VAH was defined as a V2 diameter ≤ 2 mm or an asymmetry ratio ≥ 1:1.7 in all of the 4 segments [5,6].

2.4. DWI assessment for acute infarction

The acute posterior circulation infarction (PCI) lesion was confirmed by high signal intensity on DWI with low signal intensity on apparent on diffusion coefficient (ADC).

2.5. Obtaining parameter values in the PICA territory using PWI

All the original scanning images of PWI from every patient were processed by software application GE Brainstat (Functool 9.4.05, GE healthcare). For this study we chose AIF protocol that generates processed maps based on Artery Input Functions (AIF) and Vein Output Functions (VOF). Regions of interest (ROIs) on one lateral inferior cerebellum avoiding large vessels and then their mirrored ROIs on the contralateral cerebellar hemisphere relative to a symmetrical axis were created semi-automatically, meanwhile time/intensity curve and mean parameter values of each ROI in corresponding parameter map were generated automatically.

Defined rCBF = the ratio of mean CBF obtained from the non-dominant VA side ROI and mean CBF obtained from the dominant VA side ROI. In this analogy, relative perfusion parameter values (rCBF, rCBV, rMTT and rTTP) were calculated (see Fig. 1 in detail). We also counted the number of subjects with rCBV ≤ 0.85 or rCBV ≤ 0.85. The post process of original PWI images were performed blindly to that of other clinical data, especially to the CE-MRA analysis.

2.6. Statistical analysis

Software SPSS (version 13.0, SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. Normal distribution was tested with Kolmogorov-Smirnov test. Non-normal distribution variables were presented by median (range) and tested using nonparametric test. Normal distribution variables were tested using Independent *t*-test or χ^2 (fisher's exact) test and presented as mean ± standard deviation (SD) and number (percentage) respectively. Variables having *P* value <0.05 were selected and further evaluated using multivariate logistic regression models with the forward stepwise selection method. Two-sided *P* values of <0.05 were considered to indicate statistical significance.

3. Results

A total of 187 consecutively hospitalized patients who underwent DSC-PWI because of suspect stroke. To study AWI and PWI further, 15 patients (poor PWI image, 3; without DWI or CE-MRA, 5; occlusive VA, 1; VA with significant stenosis, 4) unqualified for our study were excluded as is seen in Fig. 2. Of 172 patients that were eligible for this study, VAH was found in 57 patients (33.1%). Among the 57 patients with VAH, 46 (80.7%) had VAH on the right side and 37 (64.9%) were males. No significant difference existed in age or gender distribution between patients with or without VAH ($P > 0.05$). 26 of 57 VAH patients and 31 of 115 non-VAH patients were diagnosed acute PCI according to DWI and ADC. Among 31 VAH patients without PCI, 26 (84%) patients had VAH on the right.

Table 1 summarizes the demographic and clinical characteristics of the 58 patients with PCI and 114 patients without PCI. There were statistically significant differences in VAH, hypertension, alcoholism, smoking, and NIHSS ($P < 0.05$). Factors including VAH, hypertension, alcoholism and smoking were further evaluated using multivariate logistic regression models with the forward stepwise selection method, which indicated that VAH (OR 2.10, $P = 0.039$), hypertension (OR 2.97, $P = 0.005$), smoking (OR 2.53, $P = 0.010$) were significantly associated with the likelihood of PCI.

Table 2 shows the comparative results between PCI patients with or without VAH. No significant difference between the groups with regard to age, gender, hypertension, diabetes, coronary heart disease, alcoholism, smoking, BMI and NIHSS.

Baseline data of non-PCI patients with or without VAH with regard to age, gender, hypertension, diabetes, hyperlipidemia, alcoholism, smoking, BMI and NIHSS were equally distributed as is listed in Table 3.

Perfusion parameter ratios in PICA territory were calculated and compared between non-PCI patients with or without VAH, as is shown in Table 4. There were significant differences in the frequency of rCBF ≤0.85 and rTTP in the inferior cerebellum region between non-PCI patients with or without VAH ($P < 0.05$). It is notable that there was significant difference ($P < 0.001$) on rTTP value compared to value