Prediction of Cerebrovascular Reserve Capacity by Computed Tomography Perfusion Using 320-Row Computed Tomography

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Background: Acetazolamide loading has been the "gold standard" for evaluating cerebrovascular reserve capacity (CVRC). However, life-threatening side effects of acetazolamide have recently been reported. The aim of the study was to identify alternative methods for evaluating CVRC. *Methods:* We reviewed 6 patients who underwent both computed tomography perfusion (CTP) imaging and xenon CT (XeCT) imaging with and without acetazolamide loading during the same periods. The data were obtained as volume data using 320-row CT and applied to the automated region of interest–determining software and converted to standardized images. Correlations between CVRC and CTP parameters were analyzed by Pearson correlation coefficient analysis, and simple regression was used to assess the relationship between the data. When statistically significant, correlation between CVRC and any CTP data is identified, and cutoff points for CVRC 30% and 10% were calculated with receiver operating characteristic curves. *Results:* Of 4 CTP parameters evaluated, statistically significant correlations were observed between time to peak (TTP) by CTP and CVRC ($P < .0001$, $r = -.7228$) calculated from XeCT. The regression line using CVRC as outcome variable (y) and using TTP as predictor variable (x) was $y = -9.062x + 140.1$. The cutoff value for the TTP for CVRC less than 10% was 12.56 seconds (sensitivity of 86% and specificity of 85%) and that for CVRC less than 30% was 9.34 seconds (sensitivity of 77% and specificity of 96%). *Conclusions:* TTP calculated from CTP data correlated well with the CVRC calculated from XeCT data. These results suggest that TTP calculated from CTP could be used to estimate CVRC in patients with occlusive cardiovascular disease. **Key Words:** 320-row CT—CT perfusion—xenon CT—CVRC—TTP—automated ROI.

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Introduction

Acetazolamide loading has been the "gold standard" for evaluating cerebrovascular reserve capacity (CVRC).[1,2] However, in June 2014, an emergent notification regarding life-threatening side effects of acetazolamide was announced by 4 major academic societies in Japan related to cerebral blood flow (CBF) and metabolism. In the notification, 8 cases of major side effects including heart failure and pulmonary edema because of acetazolamide during the past 20 years were reported. Therefore, alternative methods for evaluating CVRC in patients with occlusive cardiovascular disease (CVD) are needed.

Positron emission tomography has been known to be the most effective method for measuring cerebrovascular reserve from both perfusion and metabolic data of the brain.[3] However, positron emission tomography requires expensive equipment that cannot be used everywhere. Several stimuli other than acetazolamide loading, including CO_2 inhalation and breath holding, are known to change arterial CO_2 levels and, thus, may be used for evaluating CVRC.[4,5] In addition, a few studies have been published that attempt to estimate CVRC without carbon stimuli.[6,7] In the studies, parameters for cerebral perfusion, such as mean transit time (MTT) and time to peak (TTP), were suggested to correlate well with CVRC. Cerebral perfusion parameters, such as MTT and TTP, can be obtained by data from computed tomography perfusion (CTP) imaging or perfusion-weighted images (PWIs) on magnetic resonance imaging (MRI). To our knowledge, no previous study has evaluated whether perfusion parameters by CTP can predict CVRC.

CT perfusion obtains sequential CT images during contrast-enhanced medium wash-in and washout through brain tissue.[8] Time-enhancement curves can be created in each voxel of the CT images, and software analysis of the curves provides parametric maps of cerebral perfusion.[8] Cerebral perfusion parameters, such as CBF, cerebral blood volume (CBV), MTT, and TTP, can be obtained from the study. CTP can be performed rapidly and can also be used in patients during the acute stages of stroke or in patients presenting with a change in consciousness, for example, because of cerebral vasospasm after a subarachnoid hemorrhage.[9] Four-dimensional computed tomographic angiography (4D-CTA), which enables the morphologic evaluation of cerebral arteries, can be performed simultaneously. CTP also does not require any costly equipment. CTP provides both quantitative and qualitative data that can add diagnostic value in a number of neurosurgical disorders including stroke.[8]

Here, we analyzed the correlation between CVRC calculated from the results of xenon CT (XeCT) imaging with and without acetazolamide infusion and CTP parameters to develop a method for predicting CVRC without using acetazolamide.

Patients and Methods

Patients

We retrospectively analyzed 6 adult patients with documented occlusive CVD seen at our institution (Institute of Brain and Blood Vessels, Mihara Memorial Hospital, Isesaki, Gunma, Japan) for further workup. All patients included in the present study underwent both CTP and XeCT with and without acetazolamide loading for the evaluation of cerebral hemodynamics before emergent notification in June 2014. The patient group consisted of 3 men and 3 women. The mean age was 52.8 years (range, 34-68 years). Complete medical, neurologic, and radiologic examinations were performed on all patients. Three patients with moyamoya disease (one of them was probable case), 2 patients with cervical carotid stenosis, and 1 patient with internal carotid artery stenosis (from C1 to C5 portion) were studied. Patients' characteristics are summarized in Table 1. Written informed consent for using contrast material was obtained for all patients.

CT Perfusion

CTP imaging was acquired using a 320-row CT scanner (Aquilion ONE; Toshiba, Otawara, Japan). CTP and 4D-CTA were acquired simultaneously. For data acquisition, 40 mL of contrast agent (IOPAQUE 350; Fuji Yakuhin Co., Ltd, Tokyo, Japan) was injected at 5 mL/s and chased with 30 mL of saline. First, a pulsed full-rotation scan was performed for the purpose of subtraction. Then, a continuous full-rotation scan started 6 seconds after the contrast agent was injected and continued for 21 seconds. Two seconds after the end of the continuous scan, a pulsed full-rotation scan started, with imaging occurring at 11 time points over a period of 28 seconds. A 512 × 512 matrix and a .5-mm slice thickness were used. The exposure factors were 80 kV(p) and 100 mA (for continuous scanning) or 50 mA (for pulsed scanning), and the scan time was 1 second. Volumetric CT dose index (CTDI) for the protocol is 183.1 mGy, and dose length product is 2564.4 mGy. In comparison, CTDI for routine whole-brain, noncontrast CT images using this CT scanner is 87.5 mGy. 4D-CTA data were processed by a three-dimensional workstation (Ziostation; Ziosoft, Shinjuku, Tokyo, Japan), and the development of the arterial circle of Willis and the stenosis of major arteries were assessed.

Xenon CT

XeCT imaging was acquired using the same 320-row CT scanner (Aquilion ONE; Toshiba) that was also used for CTP imaging. Patients inhaled 30% stable xenon for 3 minutes (wash-in) followed by 4 minutes of desaturation (washout) using a xenon gas inhalation system (AZ-727; Anzai Medical, Tokyo, Japan). First, a pulsed full-rotation scan was performed for subtraction at the time when inhalation began. One minute later, a pulsed