Narrowed Petrous Carotid Canal Detection for the Early Diagnosis of Moyamoya Disease

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Abstract Purpose: Patients with moyamoya disease (MMD) exhibit narrowed internal carotid arteries (ICAs) because the distal ends of the bilateral ICAs have become progressively stenosed, starting mainly in childhood. Accordingly, the petrous carotid canals in MMD patients are suspected to be more hypoplastic than those in control subjects. In this study, the diagnostic value of conventional computed tomography for MMD patients was retrospectively evaluated by comparing the caliber of the bilateral carotid canals in MMD patients with that in control subjects.

Materials and methods: Thirty-five patients with MMD (15 males, 20 females; age range/average age: 6–71 / 26.1 years old) and age- and sex-matched control subjects underwent conventional head computed tomography. The maximal petrous carotid canal diameters of the two groups were measured and compared.

Results: The maximal petrous carotid canal diameter was significantly smaller in the moyamoya patients (mean ± standard deviation [mm] = 4.70 ± 0.61) than in the control subjects (5.62 ± 0.61, \(p < 0.01\)).

Conclusion: Conventional head computed tomography revealed narrowed petrous carotid canals in the MMD patients. This basic information could be utilized to screen patients who will require further examination, especially among those with underlying MMD.

Key words: Moyamoya disease, Carotid canal, Computed tomography (CT), Magnetic resonance imaging (MRI)

Introduction

Moyamoya disease (MMD) was first reported by Takeuchi and his colleagues as hypoplasia of the bilateral internal carotid arteries (ICAs)\(^1\). Currently, the pathological features of MMD have been understood as the chronic progressive occlusion of the distal portion of the bilateral ICAs and the proximal portion of the middle and anterior cerebral arteries (MCAs and ACAs), which are the main branches within the circle of Willis\(^3\).

After the diagnostic criteria for MMD diagnosed by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were proposed in 1997, these modalities have become well-accepted noninvasive diagnostic approaches to the evaluation of MMD\(^2\). However, the major indications for MRI examination have been applied only in follow-up care for patients with repetitive and/or progressive central nervous system (CNS) manifestations. The use of MRI and MRA for diagnosing asymptomatic MMD or a first episode of MMD remains less common.

Starting in childhood, MMD patients exhibit
narrowed ICAs\textsuperscript{3). Thus, it has been suggested that the petrous carotid canals in MMD patients are more hypoplastic than those in healthy controls. If this assumption is valid, underlying MMD may be detected by estimating the extent of hypoplastic changes in the petrous carotid canal on conventional computed tomography (CT) of the head.

Watanabe and co-workers reported petrous carotid canal narrowing in MMD patients\textsuperscript{3}. However, they investigated a limited number of MMD patients in contraposition with unmatched control subjects and did not sufficiently review in detail.

The purpose of this study was to validate our hypothesis by retrospectively estimating the differences between the petrous carotid canal diameters in MMD patients compared with those in age- and sex-matched control subjects.

### Materials and methods

#### 1. Patients

The current study was retrospectively performed and its results did not have any effect on clinical practice.

From November 2003 to July 2009, the records of MMD patients treated in our institution were isolated using the electrical medical chart system. They were verified using the database in our department if they had undergone head CT examinations. Finally, 35 patients were consequently enrolled in this study. The patients were diagnosed on the basis of the MRI and MRA Guidelines for the diagnosis of MMD proposed by the Research Committee on the Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan\textsuperscript{2}. In the study, 15 males and 20 females (age range, 6-71 years old; 16 children (15 years old or less) and 19 adults (more than 15 years old); average age, 26.1) were included. They initially presented with transient ischemic attack (TIA) (n = 25), hemorrhage (n = 6; intracerebral hemorrhage (n = 4), subarachnoid hemorrhage (n = 2), cerebral infarction (n = 2), or no symptoms (n = 2). Of these 35 patients, 27 underwent revascularization surgery either on one side (n = 20) or both sides (n = 7). The patients underwent conventional head CT for TIA (n = 4), headache (n = 4), consciousness disturbance (n = 2), convulsion (n = 2), and postoperative surveillance (n = 23). Other imaging studies that were performed included head MRI and MRA in all patients.

#### 2. Control subjects

Thirty-five age- and sex-matched patients were enrolled as control subjects by the following process. In the same period as above, patients who underwent conventional head CT were selected from our department’s database. Their clinical diagnoses and neuroimaging studies were carefully checked using the electrical medical chart system. If two or more patients were favorable to be candidates, the patient having the latest head CT examination date was chosen. Conventional head CT was performed in these patients due to head injury (n = 22), headache (n = 5), TIA (n = 1), consciousness disturbance (n = 1), convulsion (n = 1), vomiting (n = 1), preoperative cerebral assessment in a patient with aortic valve stenosis (n = 1), cerebral assessment following septic shock (n = 1), and hypoglycemic attack (n = 1): none of the subjects in the control group showed any remarkable abnormalities on conventional head CT at the time of the initial examination.

#### 3. Imaging conditions

Conventional CT was performed using a clinical CT unit (Aquilion ; Toshiba Medical Systems, Ohtawara, Japan) with a 240-mm field of view (FOV): a 4-mm slice thickness was used at the infratentorial level, and an 8-mm slice thickness was used at the supratentorial level.

The MRI arm of the experiment was performed using one of three clinical MRI units: the MAGNETOM Trio A Tim System (Siemens AG, Erlangen, Germany), the MAGNETOM Avanto A
Tim System (Siemens AG, Erlangen, Germany), or the Signa Horizon (GE Healthcare Waukesha, Wisconsin, USA). The assessment of patient status was performed using four types of imaging sequences including T1-weighted imaging, T2-weighted imaging, fluid attenuated inversion recovery imaging, and 3D-time-of-flight (TOF) -MRA.

4. Imaging analyses

In order to assess the clinical status of MMD patients, the severity of intracranial arterial stenoocclusions was evaluated on MRA with Houkin’s grading system. Cerebrovascular attack (CVA) lesions were also estimated on MRI. Those estimations were performed by a single observer (T.N., with 6 years of experience in neuroradiology).

The CT images were generated using a brain window algorithm. The estimation of CT images was carried out using a bone window (window level / width (HU) = 500 / 2000) on a computer viewer system (ViewR version 1.08, Yokogawa Electric Corporation, Tokyo, Japan) and a 54-cm class color LCD monitor (Radioforce R22, EIZO NANAO CORPORATION, Ishikawa, Japan). Three measurements were evaluated on CT, including the petrous carotid canal diameter and the transverse and anteroposterior diameters of the skull. The maximal diameter of the petrous carotid canal was measured at 10-fold magnification on the viewer system. The transverse diameter of the skull was measured at the level of visualization of the cerebral peduncle instead of at the largest level because making accurate measurements was difficult in some MMD patients who had undergone previous craniotomy procedures for revascularization surgery. The maximal anteroposterior diameter of the skull was measured at the widest level. As noted above, according to the CT imaging conditions, the petrous carotid canal, the transverse diameter, and the anteroposterior diameter were measured on CT with 4-, 8-, and 8-mm slice thicknesses, respectively. These data were independently collected by 3 observers (T.N., with 6 years of experience in neuroradiology; S.M., with 3 years of experience in radiology; and M.O., with 2 years of experience in radiology, respectively). The average values of these measurements in each object were used for the analysis.

The cross-sectional index of the skull was calculated using the transverse diameter multiplied by the anteroposterior diameter. This was used as an index of the skull size, which might have affected the diameter of the petrous carotid canal. The carotid canal cross-sectional index was also calculated according to the following formula: \( (A^2 + B^2) / \) (skull cross-sectional index), where A and B were the right and left diameters of the petrous carotid canals, respectively. This index represented the correction value of the total bilateral cross-sectional areas corrected by skull cross-sectional index.

5. Evaluation items

(a) Houkin’s staging and CVA lesions of MMD patients

Houkin’s staging and CVA lesions were clarified in 35 MMD patients.

(b) Interobserver agreement on measurements and consistency of average values

The intraclass correlation coefficient (ICC) was determined for each of the petrous carotid canal diameters and the transverse and anteroposterior diameters of the skull, in order to evaluate the level of interobserver agreement of measurement values (intraclass correlation case 3, with 1 judgment : ICC [3, 1]) and the assessment with the consistency of the average values (intraclass correlation case 3, with 3 judgments : ICC [3, 3]) as evaluated by the 3 observers. Landis’ judgment standard was adopted to roughly determine the level : values > 0.8 were considered to suggest close to perfect agreement, values > 0.6 showed substantial agreement, values > 0.4 showed moderate agreement, values > 0.2 showed fair agreement, and values > 0 showed negligible agreement.
agreement\(^6\).

(c) Petrous carotid canal diameter, skull cross-sectional index, and carotid canal cross-sectional index

The petrous carotid canal diameters, the skull cross-sectional indices, and the carotid canal cross-sectional indices were clarified and statistically compared between MMD patients vs. control subjects using Student’s-t test with a significance level of 0.05.

In order to assess the effect of age, MMD patients and control subjects were stratified into children (15 years of age or less) and adults (more than 15 years of age). The 3 parameters were also evaluated among those subgroups in the same way as above.

Results

Figures 1 and 2 show two representative cases of MMD and age- and sex-matched control cases.

Fig. 1 An 11-year-old boy with childhood-onset MMD (MRA grade: right side/ left side = 3/3). He had an initial TIA of the right upper extremity during early elementary school, and underwent right cerebral revascularization surgery at age 11. The bottom-to-top projection MRA–maximum intensity projection (MIP) image shows poor visualization of the distal ICAs and proximal MCAs bilaterally (A). CT with the bone window shows the narrowed diameters of the bilateral petrous carotid canals (right side/ left side = 3.85/3.72 (mm)) (B; parallel lines on both sides) compared to those of a control case (right side/ left side = 5.74/5.90 (mm)) (C; parallel lines on both sides).

(A) (B) (C)

Fig. 2 A 24-year-old female with adult-onset MMD (MRA grading: right side / left side = 1/1). This patient had an initial TIA of the right upper extremity at age 24 years and was managed conservatively. The bottom-to-top projection MRA–MIP image shows poor visualization of the distal ICAs, proximal MCAs, and ACAs bilaterally (A). CT with the bone window shows the narrowed diameters of the bilateral petrous carotid canals (right side/ left side = 3.85/4.71 (mm)) (B; parallel lines on both sides) compared to those of a control case (right side/ left side = 5.37/6.04 (mm)) (C; parallel lines on both sides).

(A) (B) (C)
(a) Houkin’s staging and CVA lesions of MMD patients

All patients underwent MRI and MRA. The MRA study revealed the following Houkin’s MRA grading results: (right side/left side): grade 1 (n = 3/2), grade 2 (n = 19/16), grade 3 (n = 13/17), and grade 4 (n = 0/0). The MRI study revealed the following numbers of CVA lesions: none (n = 15/15), ischemic small CVA lesion (longest diameter, < 3 cm) (n = 16/13), ischemic large CVA lesion (longest diameter, > 3 cm) (n = 3/4), intraventricular hemorrhage (n = 0/1), and subarachnoid hemorrhage (n = 1/2).

(b) Interobserver agreement on measurements and consistency of average values

The interobserver agreements on measurements of the petrous carotid canal diameters, skull cross-sectional indices, and carotid canal cross-sectional indices were judged to be substantial or almost perfect (ICC [3, 1] = 0.64, 0.88, and 0.91, respectively). The consistency of the average values of those 3 measurements was judged to be almost perfect (ICC [3, 3] = 0.84, 0.94, and 0.97, respectively).

(c) Petrous carotid canal diameter, skull cross-sectional index, and carotid canal cross-sectional index

Table 1 shows the results of the petrous carotid canal diameters, the skull cross-sectional indices, and the carotid canal cross-sectional indices in all subjects, the young or adult groups of MMD patients and the control subjects. Figure 3 shows the relationships between ages vs. petrous carotid canal diameters, ages vs. skull cross-sectional indices, and ages vs. carotid canal cross-sectional indices in the total groups of MMD patients and control subjects, respectively.

The petrous carotid canal diameters, the skull cross-sectional indices, and the carotid canal cross-sectional indices in MMD patients vs. control subjects (average ± standard deviation) were 4.70 ± 0.61 (mm) vs. 5.62 ± 0.61 (mm), 217 ± 18 (cm³) vs. 216 ± 15 (cm³), and 20.8 ± 4.8 vs. 29.7 ± 6.1, respectively. Both the petrous carotid canal diameters and the carotid canal cross-sectional indices of MMD patients were significantly smaller than those of the control subjects (p < 0.01), although no difference was observed in the skull cross-sectional indices (p = 0.848) between the two groups. The differences showed the same tendencies in both youths and adults between MMD patients and control subjects.

On the other hand, both the petrous carotid canal diameters and the carotid canal cross-sectional indices of young MMD patients were significantly smaller than those of adult MMD patients (p < 0.01) although these parameters were not significantly different between the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Results of Petrous carotid canal diameter, skull cross-sectional index, and carotid canal cross-sectional index between MMD patients and control subjects.</th>
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<td></td>
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<tr>
<td>Number of patients</td>
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<tr>
<td>Petrous carotid canal diameter (average ± standard deviation [mm])</td>
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<tr>
<td>MMD patients</td>
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<td>Normal subjects</td>
<td>5.6 ± 0.6</td>
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<tr>
<td>Skull cross-sectional index (average ± standard deviation [cm³])</td>
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<tr>
<td>MMD patients</td>
<td>217 ± 18</td>
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<tr>
<td>Normal subjects</td>
<td>216 ± 15</td>
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<tr>
<td>Carotid canal cross-sectional index (average ± standard deviation [x10⁴ no units])</td>
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<tr>
<td>MMD patients</td>
<td>20.8 ± 4.8</td>
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<tr>
<td>Normal subjects</td>
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* P < 0.001
young and adult groups in the control subjects.

Discussion

Our results might suggest that MMD patients could be stratified at an early stage of the disease using conventional head CT, which is a simple imaging tool for evaluating CNS disorders. Head CT might be performed in patients with nonspecific CNS symptoms such as TIA, catalectic attack, epilepsy, or head injury. All of these symptoms or diseases can affect MMD patients during childhood and thereafter.

While head digital subtraction angiography (DSA) is the diagnostic standard for MMD, it can cause rare but serious complications. Moreover, in pediatric patients, DSA requires general anesthesia. Head MRI and MRA are non-invasive imaging studies and they can provide helpful information about infarction, hemorrhage, and perfusion, in addition to vascular stenoocclusive findings. However, head MRI and MRA can be considered invasive because they may require

![Fig. 3 Scatter plots show age vs. petrous carotid canal diameter (A), age vs. skull cross-sectional index (B), and age vs. carotid canal cross-sectional index (C). Regression lines are shown in all figures in order to visually demonstrate the differences between groups. Chart (A) shows that the carotid canal diameters in MMD patients (triangles) are significantly smaller than those in control subjects (circles) ($y_1 = 0.041x_1 + 4.315; y_2 = 0.011x_2 + 5.318; y_1 = \text{age of MMD patient}, x_1 = \text{petrous carotid canal diameter of MMD patient}, y_2 = \text{age of control subject}, x_2 = \text{petrous carotid canal diameter of control subject}$). On the other hand, Chart (B) shows that there were no significant differences in skull cross-sectional indices between MMD patients (triangles) and control subjects (circles) ($y_3 = 0.2677x_3 + 209.71; y_4 = 0.0029x_4 + 215.86; y_3 = \text{age of MMD patient}, x_3 = \text{skull cross-sectional index of MMD patient}, y_4 = \text{age of control subject}, x_4 = \text{skull cross-sectional index of control subject}$). However, Chart (C) shows that the carotid canal cross-sectional indices in MMD patients are significantly smaller than those in control subjects ($y_5 = 0.0959x_5 + 18.258; y_6 = 0.1232x_6 + 26.444; y_5 = \text{age of MMD patient}, x_5 = \text{carotid canal cross-sectional index of MMD patient}, y_6 = \text{age of control subject}, x_6 = \text{carotid canal cross-sectional index of control subject}$). These results suggest that the carotid canal cross-sectional index in MMD patients is smaller than that in control subjects, regardless of the skull cross-sectional index.
sedation in some pediatric patients. In addition, head MRI and MRA are used as secondary screening modalities for diagnosing CNS disorders. Again, it should be emphasized that head CT is considered to be a useful screening modality in this context, and a finding of petrous carotid canal stenosis should be an indication to perform additional examinations to assess risk. Of course, head CT scan should only be done when clinically justified. A recent report showed that the radiation exposure due to CT scans in childhood has a subsequent risk of brain tumors and leukemia. Pearce and co-workers reported that the cumulative ionizing radiation doses from 23 head CTs (ie, ~60 mGy) could almost triple the risk of brain tumors and those from 5.10 head CTs (~50 mGy) could triple the risk of leukemia. With the increasing use of CT worldwide, particularly within this young population, knowledge of the risks based on empirical data will be crucial to assess safety in relation to the benefits that CT provides, following the “as low as reasonably achievable” (ALARA) principle.

It has been suggested that ICA stenosis begins in childhood in MMD patients. Early-onset ICA stenosis can lead to petrous carotid canal stenosis, since bony carotid canal development is thought to represent ICA development. If this hypothesis is correct, the onset of ICA stenosis, or rather the developmental onset of MMD, might be estimated for individual patients based on what is known about the normal correlation between age and petrous carotid canal diameter. Moreover, the current study clarified the significant difference in petrous carotid canal diameters between young and adult MMD patients. This might suggest that young MMD patients have an earlier onset or show faster progress of intracranial arterial stenosis than adults. However, further research needs to be performed in order to confirm this hypothesis.

Interestingly, we found no difference between MMD patients and the control subjects in terms of the skull cross-sectional index. This result led us to suspect that there might be no low-growth cerebrum in MMD patients. However, further investigations are needed to validate this speculation as well.

Watanabe and co-workers reported that 11 adult MMD patients exhibited bilateral petrous carotid canal stenoses. However, their study has two limitations. First, their study assessed a relatively small number of patients. This raises a concern about the accuracy of the study. Second, the healthy subjects in the control group did not match the subjects in the MMD group. Accordingly, the control group may have been subject to selection bias. In contrast to these points, we assessed a relatively large patients and mitigated the potential selection bias of the control group by performing an age- and sex-matched case control study. In addition, we reviewed the data of three observers for each subject to assure the credibility of the data. Furthermore, we incorporated the assessment of the skull–cross–sectional index and carotid canal cross-sectional index in the comparative review.

The present study had some limitations. The petrous carotid canal diameters were analyzed regardless of the patient’s history of revascularization surgery, sex, age at first onset, and disease severity. It remains unknown whether or not any of these factors affect petrous carotid canal diameter, but if any of them do, the mechanism of pathogenesis related to each relevant factor would also be of great interest. Future investigation will hopefully provide important insight into the underlying causes of MMD. In the current study, CT imaging with a 4-mm slice thickness was used to measure the petrous carotid canal diameters. While estimations based on conventional CT were meaningful considering the aim of the present study, some inaccuracy in measurement was evident due to the partial volume effect. It is important to propose a more accurate cut-off value for the petrous carotid canal diameter by performing measurements on reconstructed images, acquired perpendicular to the petrous
carotid canal axis, which could be generated by multi-detector row CT.

In conclusion, our series revealed that the narrowed petrous carotid canal diameter demonstrated on conventional head CT can be helpful in identifying MMD patients.

Reference


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もやもや病診断における頸動脈管径測定の有用性に関する検討

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目的：もやもや病は幼少期から内頸動脈終末部が進行性に狭窄する。もやもや症候例では頸動脈管径が健康者と比較して、より低形成となることが考えられる。本後向き研究では頭部 CT 検査で頸動脈管径を測定することによるもやもや病早期診断の可能性につき検討した。

対象と方法：25 例のもやもや症候例群（男性 15 例、女性 20 例、年齢: 6-71 歳、平均 26.1 歳）と明かなる頭蓋内病変を認めない性別と年齢を一致させ、頭部 CT 検査を受けた症例を対照群とした。

頸部 CT 検査で両群の頸動脈管径を測定し、両群間を比較検討した。

結果：もやもや症候群の頸動脈管径（平均 4.70 ± 0.61mm）は対照群（平均 5.62 ± 0.61mm, p < 0.01）と比較して有意な狭小化が示された。

考察：頭部単純 CT 検査で頸動脈管径を評価することにより、もやもや病の早期検出をできる可能性があると考えられた。

結論：もやもや病早期診断における頸動脈管径測定の有用性が示唆された。