Cerebellar Cortical Infarct Cavities
Correlation With Risk Factors and MRI Markers of Cerebrovascular Disease

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Background and Purpose—Small cerebellar infarct cavities have been recently found on magnetic resonance imaging (MRI) to preferentially involve the cerebellar cortex, but epidemiological studies are lacking. We aimed to determine the prevalence and risk factor profiles of cerebellar cortical infarct cavities (≤1.5 cm) as well as their association with MRI markers of cerebrovascular disease and functioning.

Methods—We analyzed the 1.5 Tesla MRI of 636 patients (mean age, 62±9 years; 81% men) from the Second Manifestations of Arterial Disease—Memory, Depression and Aging (SMART-Medea) study. Logistic regression analyses were performed to estimate the associations of age, sex, vascular risk factors, MRI markers of cerebrovascular disease, and functioning with cerebellar cortical cavities, adjusted for age and sex.

Results—Cerebellar cortical infarct cavities occurred on MRI in 10% of patients and were significantly associated with age, intima-media thickness (odds ratio [OR], 2.0; 95% confidence interval [CI], 1.1–3.7), high levels of homocysteinemia (OR, 1.8; 95% CI, 1.0–3.3), cortical infarcts (OR, 2.9; 95% CI, 1.6–5.4), gray matter lacunes of presumed vascular origin (OR, 3.0; 95% CI, 1.6–5.8), brain stem infarcts (OR, 5.1; 95% CI, 1.9–13.6), and decreased brain parenchymal fraction (OR, 0.84; 95% CI, 0.74–0.94), but not with white matter hyperintensities (OR, 1.2; 95% CI, 0.8–1.8) or white matter lacunes of presumed vascular origin (OR, 1.1; 95% CI, 0.5–2.5). They were also associated with worse physical functioning (OR 0.96; 95% CI, 0.94 to 0.99) but not with mental functioning.

Conclusions—Cerebellar cortical infarct cavities are far more common than previously assumed based on symptomatic case series and are associated with markers of atherothromboembolic cerebrovascular disease. (Stroke. 2015;46:3154-3160. DOI: 10.1161/STROKEAHA.115.010093.)

Key Words: atherosclerosis ■ brain stem ■ cerebrovascular disorders ■ magnetic resonance imaging ■ white matter

With the aging population and high availability of imaging studies, it is estimated that most persons now at least have 1 computed tomography or magnetic resonance imaging (MRI) study of the brain during life. Knowledge about commonly observed incidental imaging findings is therefore mandatory. In the cerebrum, incidental infarcts are commonly seen on MRI, with a prevalence ranging from 20% in healthy elderly to over 50% in patients with vascular or ischemic cerebrovascular disease.1–3 They have considerable impact as they are associated with increased risks of stroke, cognitive dysfunction, and dementia.4,5

Cerebellar infarcts have been well studied before in patients presenting with clinical symptoms.6–9 Large and small cerebellar infarcts have been found to be essentially of atherothromboembolic origin, with the site and size of the infarct depending on the responsible blood clot.10 Although small cerebellar infarcts <2 cm are seen in >90% of symptomatic patients presenting with multiple cerebellar infarcts on MRI,11,12 many small cerebellar infarcts may remain clinically occult, especially if occurring in isolation.13,14,15 Still, the same infarcts may be detected later on as an incidental infarct cavity on imaging studies.13–15 Recent studies have shown that the overwhelming majority of such cerebellar infarct cavities involve the cortex, as opposed to the much rarer lacunes (of presumed vascular origin) affecting the deep cerebellum.13,15 In addition, cerebellar cortical cavities have recently been confirmed to be of ischemic origin and to be easily identified and characterized on MRI scans.13,15 Nevertheless, epidemiological studies investigating these cerebellar cortical infarct cavities are lacking.

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The aim of this study was to investigate the occurrence and determinants of cerebellar cortical infract cavities on brain MRI in a cohort of patients with proven vascular disease. In addition, we aimed to correlate the presence of these cavities with MRI markers of cerebrovascular disease and with physical and mental functioning.

Materials and Methods

Subjects

Data were used from the Second Manifestations of Arterial Disease-Memory, Depression and Aging (SMART-Medea) study, a cohort study in patients with a history of arterial disease.16,17 The SMART-Medea study is an ancillary study to the SMART-MR study, which has been described in more detail elsewhere.18,19 In brief, between May 2001 and December 2005, 1309 patients newly referred to the University Medical Center Utrecht for treatment of symptomatic atherosclerotic disease (manifest coronary artery disease, cerebrovascular disease, peripheral arterial disease, or abdominal aortic aneurysm) without MRI contraindications were enrolled in the SMART-MR study. Exclusion criteria were age >80 years, diagnosis of a terminal malignancy, lack of independence in daily activities (Rankin scale >3), and lack of fluency in Dutch or referral back to the referring specialist. Between April 2006 and May 2009, 710 participants had follow-up measurements, including 3-dimensional (3D) T1-weighted MR images to assess hippocampal volumes as part of the SMART-Medea study.

During a 1 day visit to the University Medical Center Utrecht, a physical examination, ultrasonography of the carotid arteries, blood and urine samplings, neuropsychological and depression assessment, and a 1.5-Tesla brain MRI scan were performed. Questionnaires were used for assessing demographics, risk factors and medical history, medication use, functioning, psychosocial vulnerability and stress factors, and depressive symptoms.

The SMART-MR and SMART-Medea studies were approved by the ethics committee, and written informed consent was obtained from all participants.

Study Sample

Of the 710 patients included, 44 did not have an MRI scan and 30 did not have adequate data for segmentation. Thus, for this study, we included the 636 patients in whom an adequate 3D T1 Fast Field Echo sequence was performed,20 which is used for optimal characterization of cerebellar cavities, as discussed elsewhere.13,15

Magnetic Resonance Protocol

The MR investigations were performed on a 1.5-Tesla whole body system (Gyroscan ACS-NT, Philips Medical Systems, Best, The Netherlands). The protocol consisted of a transversal T1-weighted gradient-echo sequence (repetition time (TR)/echo time (TE): 235/2 ms; flip angle, 80°), a transversal proton density- and T2-weighted turbo spin echo sequence (TR/TE: 2200/11 ms and 2200/100 ms; turbo factor 12), a transversal T2-weighted fluid attenuating inverse recovery (FLAIR) sequence (TR/TE/inversion time: 6000/100/2000 ms), and a transversal inversion recovery sequence (TR/TE/ inversion time: 2900/22/410 ms). All former sequences were acquired with the following MRI sequence parameters: field of view, 230 mm x 230 mm; matrix size, 180 x 256; slice thickness, 4.0 mm; slice gap, 0.0 mm; 38 slices. In addition, a 3D T1-weighted Fast Field Echo was acquired with the following MRI sequence parameters: TR/TE: 7.0/3.2 ms; flip angle 8°, field of view, 240 mm; matrix size, 240 x 256; slice thickness, 1.0 mm; no gap; 170 slices.

Brain Segmentation

We used the T1-weighted gradient-echo, inversion recovery sequence and FLAIR sequence for brain segmentation. The probabilistic segmentation technique has been described elsewhere.21 The segmentation program distinguishes cortical gray matter, white matter, sulcal and ventricular cerebrospinal fluid, and WMH. The results of the segmentation analysis were checked visually for the presence of infarcts and adapted if necessary to make a distinction between WMH and infract volumes. Total brain volume was calculated by summing the volumes of gray and white matter and existing volumes of WMHs and infarcts. All volumes cranial to the foramen magnum were included. Thus, the total brain volume includes the cerebrum, brain stem, and cerebellum. Total intracranial volume was calculated by summing total brain volume, sulcal volume, and ventricular cerebrospinal fluid volume.

Measurement of Cerebral Blood Flow

Postprocessing of flow measurements was performed blinded to the clinical or brain characteristics of the patient. For each vessel, the spatial and time-averaged flow velocity was calculated from the phase-difference images by manually drawing a region of interest around the vessel.22 The average flow velocity in each vessel was multiplied by the cross-sectional area of the pixels in the region of interest to obtain the volume of flow rate. Good agreement between the repeated volume flow rate measurements was shown in our group, with a 5% coefficient of variation.21 The flow through the left and right internal carotid arteries and basilar artery were assessed and summed up to calculate the total cerebral blood flow (tCBF) expressed in mL/min. Because interindividual differences in CBF can be partly attributed to differences in brain volume, we expressed tCBF per 100 mL brain tissue by dividing the tCBF by the total brain volume (mL) and multiplying this by 100 to obtain parenchymal CBF.24

Image Analysis

Cerebrum and Brain Stem

The cerebrum was visually searched for infarcts by 2 trained investigators and a neuroradiologist to make a distinction between WMH and brain infarcts. Raters were blinded for the history and diagnosis of the patient. Discrepancies in rating were reevaluated in a consensus meeting. Lacunes of presumed vascular origin and infarcts were defined as focal hyperintensities on T2-weighted images (T2WI) of at least 3 mm in diameter, whereas dilated perivascular spaces were distinguished from infarcts and lacunes of presumed vascular origin on the basis of their location, form, and the absence of gliosis. Lacunes of presumed vascular origin and infarcts located in the white matter also needed to be hypointense on T1- and FLAIR-weighted images to distinguish them from WMH. Lacunes of presumed vascular origin were 3 to 15 mm in diameter and located in the subcortical white matter or deep gray matter (thalamus or basal ganglia). Large subcortical infarcts were sized >15 mm and were not confluent with cortical infarcts. Supratentorial infarcts included any cortical or large subcortical infarct, as well as all lacunes of presumed ischemic origin in deep gray or white matter. WMH volumes were expressed as percentage of intracranial volume. Large WMH volume was defined as the highest quintile of WMH volume.

Cerebellum

The cerebellum was visually searched for infarcts including cortical cavities by a neuroradiologist (J.H.). For the analysis of number and location of cerebellar infarcts, raters were blinded for the history and diagnosis of the patient. Discrepancies in rating were reevaluated in a consensus meeting with another neuroradiologist (J.H.). For the analysis of number and location of cerebellar infarcts, transverse T2WI were used as a screening modality25 because these are known to be more sensitive than FLAIR for the evaluation of the posterior fossa.26 Infarcts detected on T2WI were correlated with FLAIR- and 3D T1-weighted images to assess the presence of cavitation (Figures 1 and 2). Cavitation was present if intraleSIONal fluid intensity on T2WI could be confirmed on FLAIR- or 3D T1-weighted images. The longest and shortest diameters of each infract were measured on axial T2WI, and the mean axial diameter was calculated as the mean of both values. For each infract encountered, the involvement of cortex and white matter was...
evaluated on 3D T1-weighted images (Figures 1 and 2). Cerebellar cortical (infarct) cavities were defined as cavities ≤1.5 cm involving the cerebellar cortex.13,15

Vascular Risk Factors
During the patient’s baseline visit to the medical center, an overnight fasting venous blood sample was taken to determine glucose and lipid levels. Height and weight were measured without shoes and heavy clothing, and the body mass index was calculated (kg/m²). Systolic and diastolic blood pressures (mm Hg) were measured twice with a sphygmomanometer, and the average of the two measures was calculated. Hypertension was defined as mean systolic blood pressure ≥160 mm Hg or mean diastolic blood pressure ≥ 95 mm Hg or self-reported use of antihypertensive drugs. Diabetes mellitus was defined as glucose ≥7.0 mmol/L or self-reported use of oral antidiabetic drugs or insulin. Total cholesterol was defined as a continuous variable expressed in mmol/L. Smoking habits and alcohol intake were assessed with questionnaires. Pack years of smoking were calculated, and alcohol intake was categorized as never, former, or current. Patients who had quit drinking during the past year were assigned to the category current alcohol intake. Hyperhomocysteinemia was defined as the highest quintile of homocysteine level versus the 4 lower quintiles. Ultrasonography was performed to measure the intima-media thickness (IMT, mm) in the left and right common carotid arteries, represented by the mean value of 6 measurements. The highest quintile versus lower 4 quintiles of IMT were defined for data analysis.

Physical and Mental Functioning
Global cognitive functioning was measured with the Mini-Mental State Examination.27 Patients completed the Short Form-12 (SF-12),28 a shortened version of the SF-36 Medical Outcomes Study Health Survey,29 to measure health-related quality of life. The SF-12 questionnaire includes 1 or 2 items from each of the 8 health summary scales of the SF-3630 and enables calculation of the Physical and Mental Component Summary scales. The SF-12 summary scales are positively scored and normalized to a general population mean of 50 with SD of 10. Higher SF-12 scores indicate better health-related quality of life; a positive change in SF-12 scores indicates an improvement and a negative change indicates a deterioration in health-related quality of life. Because of its brevity, the SF-12 is considered advantageous over the SF-36 for large studies focusing on overall physical and mental functioning.30

Data Analysis
Baseline characteristics were calculated for the study sample (n=636). Next, logistic regression analysis was performed to estimate the associations of age, sex, and vascular risk factors (history of hypertension, systolic and diastolic blood pressure, cholesterol level, homocysteine level, diabetes mellitus, smoking, and alcohol intake) with presence or absence of cerebellar cortical cavities, adjusted for age and sex. Second, logistic regression analysis was performed to estimate the association between MRI markers of cerebrovascular disease (cortical infarcts, large subcortical infarcts, lacunes of presumed vascular origin in deep gray and white matter, and cerebral blood flow) with presence or absence of cerebellar cortical cavities, adjusted for age and sex. In addition, the latter analyses were repeated for patients with multiple cerebellar cortical infarct cavities. Third, linear regression analysis was used to investigate whether presence of cerebellar cortical infarct cavities (dependent variable) was associated with changes in physical and mental functioning (independent variable), corrected for age and sex. Statistical analyses were performed with SPSS 20.0 (IBM Corp, Armonk, NY).

Results
Baseline characteristics of the study are presented in Table 1. The mean age of the population was 62±9 years (range, 33–83

Figure 1. A, Axial T2-weighted image and (B) axial fluid attenuating inverse recovery show a cerebellar cortical infarct cavity (cross mark) in the right cerebellar hemisphere, whereas its cortical location is best seen on the sagittal reconstruction of the 3-dimensional T1-weighted images (C). The cavity shows signal intensities equal to cerebrospinal fluid on all magnetic resonance imaging sequences (A–C). Notice the associated large subcortical infarct at the parieto-occipital junction (C).

Figure 2. A, Axial T2-weighted image and (B) axial fluid attenuating inverse recovery (FLAIR) show a cerebellar cortical infarct cavity (arrow) in the right cerebellar hemisphere of a 60-year-old man, occurring in combination with an excavated pontine infarction (dashed arrows). The hyperintense borders of both cavities on FLAIR are indicative of gliosis (B). Notice the cortical location of the lesion on the sagittal reconstruction of the 3-dimensional T1-weighted images (C).
years) and 80.8% were men. The majority of the population had coronary artery disease, which was present in 64.2% at baseline. One or more cerebellar cortical cavities were observed in 61 (9.6%) of patients, whereas cerebellar infarcts all together, including cerebellar cortical infarct cavities, were observed in 11% of patients.

Age (odds ratio [OR], 1.04 per year increase; 95% confidence interval [CI], 1.01–1.07) was associated with cerebellar cortical cavities, whereas sex was not. Table 2 shows the results of the logistic regression analyses for the associations of vascular risk factors and MRI markers with cerebellar cortical cavities after adjustment for age and sex. A positive history of cerebrovascular disease was significantly associated with presence of cerebellar cortical cavities (OR, 3.1; 95% CI, 1.8–5.4). Hyperhomocysteinemia was also significantly associated with cerebellar cortical cavities (OR, 1.8; 95% CI, 1.0–3.3) as was with a high IMT (OR, 2.0; 95% CI, 1.1–3.7). Other vascular risk factors were not significantly associated with cerebellar cortical cavities.

Cortical infarcts in the cerebrum (OR, 2.9; 95% CI, 1.6–5.4), supratentorial infarcts in general (OR, 2.9; 95% CI, 1.6–5.3), and brain stem infarcts (OR, 5.1; 95% CI, 1.9–13.6) were significantly associated with cerebellar cortical cavities after correction for age and sex. Cerebral lacunes of presumed vascular origin were also significantly associated with cerebellar cortical cavities (OR, 2.4; 95% CI, 1.3–4.2) after correction for age and sex. After subdividing cerebral lacunes according to location, lacunes in the deep gray matter were more strongly and significantly associated with cerebellar cortical cavities (OR, 3.0; 95% CI, 1.6–5.8), whereas lacunes of presumed vascular origin in white matter were not (OR, 1.1; 95% CI, 0.5–2.5).

Brain parenchymal fraction was significantly associated with the presence of cerebellar cortical cavities (OR, 0.84; 95% CI, 0.74–0.94), which persisted after additional adjustments for IMT (OR, 0.85; 95% CI, 0.75–0.95) or supratentorial infarcts (OR, 0.87; 95% CI, 0.77–0.98), but lost statistical significance after additional adjustments for both IMT and supratentorial infarcts (OR, 0.89; 95% CI, 0.79–1.01). No significant associations were found between cerebellar cortical cavities and large volume of WMH (OR, 1.2; 95% CI, 0.8–1.8) or parenchymal total cerebral blood flow (OR, 1.0; 95% CI, 1.0–1.0).

Presence of cerebellar cortical infarct cavities was significantly associated with worse physical functioning (OR 0.96; 95% CI, 0.94 to 0.99), whereas it was not associated with mental functioning (OR 0.98; 95% CI, 0.94 to 1.02) or Mini-Mental State Examination (OR 0.97; 95% CI, 0.8 to 1.1).

Twenty-four patients (3.8%) showed multiple cerebellar cortical infarct cavities, with a maximum of 10 in 1 patient.

Table 1. Baseline Characteristics of the Study Sample

<table>
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<tr>
<th>Study Sample</th>
<th>No CCC (90.4%)</th>
<th>CCC (9.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62±9</td>
<td>61.2±9.5</td>
</tr>
<tr>
<td>Men, %</td>
<td>80.8</td>
<td>80.2</td>
</tr>
<tr>
<td>Vascular risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pack years of smoking, n=633</td>
<td>19.6</td>
<td>19.5</td>
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<tr>
<td>Present alcohol consumption, %</td>
<td>79.0</td>
<td>79.0</td>
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<tr>
<td>History of arterial hypertension, %, n=631</td>
<td>48.3</td>
<td>47.2</td>
</tr>
<tr>
<td>Cholesterol, mmol/L, n=628</td>
<td>4.8</td>
<td>4.8</td>
</tr>
<tr>
<td>High homocysteine level, % (highest quintile, &gt;15.9 µmol), n=631</td>
<td>20.0</td>
<td>18.6</td>
</tr>
<tr>
<td>High IMT, % (highest quintile, &gt;1.11 mm), n=631</td>
<td>18.9</td>
<td>17.3</td>
</tr>
<tr>
<td>High IMT, % (highest quintile, &gt;1.11 mm), n=631</td>
<td>18.9</td>
<td>17.3</td>
</tr>
<tr>
<td>History of diabetes mellitus, %</td>
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<td>15.0</td>
</tr>
<tr>
<td>Vascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of cerebrovascular disease at follow-up, %</td>
<td>25.3</td>
<td>22.8</td>
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<tr>
<td>Cerebrovascular markers and measures on MRI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supratentorial infarct, %</td>
<td>14.0</td>
<td>12.2</td>
</tr>
<tr>
<td>Cerebral cortical infarct, %</td>
<td>13.2</td>
<td>11.5</td>
</tr>
<tr>
<td>Large subcortical cerebral infarct, %</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>Lacune of presumed vascular origin, %</td>
<td>20.8</td>
<td>18.8</td>
</tr>
<tr>
<td>White matter lacunes, %</td>
<td>9.9</td>
<td>9.6</td>
</tr>
<tr>
<td>Gray matter lacunes, %</td>
<td>11.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Brain stem infarcts, %</td>
<td>3.3</td>
<td>2.4</td>
</tr>
<tr>
<td>Total WMH, % ICV, n=609</td>
<td>0.26</td>
<td>0.25</td>
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<tr>
<td>Brain parenchymal fraction, % of ICV, n=609</td>
<td>78.4</td>
<td>78.5</td>
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<tr>
<td>Parenchymal total CBF, mL/min/100 mL, n=587</td>
<td>50.9</td>
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<td>Basilar artery flow, mL/min/100 mL, n=618</td>
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CBF indicates cerebral blood flow; CCC, cerebellar cortical (infarct) cavity; ICV, intracranial volume; IMT, intima-media thickness; MRI, magnetic resonance imaging; and WMH, white matter hyperintensities.
Vascular risk factors and cerebrovascular markers and measures on MRI as determinants of cerebellar cortical cavities, corrected for age and sex

<table>
<thead>
<tr>
<th>Measure</th>
<th>Odds Ratio</th>
<th>95% CI</th>
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<tr>
<td>Age, per year increase</td>
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<td>1.01–1.07</td>
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<td>Sex, men</td>
<td>0.6</td>
<td>0.3–1.3</td>
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<tr>
<td>Pack years of smoking, per year increase</td>
<td>1.0</td>
<td>1.0–1.0</td>
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<tr>
<td>Present alcohol consumption, yes/no</td>
<td>1.0</td>
<td>0.7–1.5</td>
</tr>
<tr>
<td>History of arterial hypertension, yes/no</td>
<td>1.6</td>
<td>0.9–2.8</td>
</tr>
<tr>
<td>Diabetes mellitus, yes/no</td>
<td>1.4</td>
<td>0.7–2.8</td>
</tr>
<tr>
<td>Cholesterol level, per mmol/L increase</td>
<td>0.8</td>
<td>0.6–1.1</td>
</tr>
<tr>
<td>High homocysteine level, highest quintile vs rest</td>
<td>1.8</td>
<td>1.0–3.3</td>
</tr>
<tr>
<td>IMT, highest quintile vs rest</td>
<td>2.0</td>
<td>1.1–3.7</td>
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</tbody>
</table>

Vascular disease

<table>
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<tr>
<th>Measure</th>
<th>Odds Ratio</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>History of cerebrovascular disease</td>
<td>3.1</td>
<td>1.8–5.4</td>
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<tr>
<td>Cerebrovascular markers and measures on MRI</td>
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<td>1.6–5.4</td>
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<tr>
<td>Cortical infarcts, yes/no</td>
<td>4.3</td>
<td>0.7–24.7</td>
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<tr>
<td>Lacunes of presumed vascular origin, yes/no</td>
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<td>1.3–4.2</td>
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<td>Gray matter lacunes, yes/no</td>
<td>3.0</td>
<td>1.6–5.8</td>
</tr>
<tr>
<td>White matter lacunes, yes/no</td>
<td>1.1</td>
<td>0.5–2.5</td>
</tr>
<tr>
<td>Supratentorial infarct, yes/no</td>
<td>2.9</td>
<td>1.6–5.3</td>
</tr>
<tr>
<td>Brain stem infarct, yes/no</td>
<td>5.1</td>
<td>1.9–13.6</td>
</tr>
<tr>
<td>White matter hyperintensities, highest quintile</td>
<td>1.2</td>
<td>0.8–1.8</td>
</tr>
<tr>
<td>Brain parenchymal fraction, % of ICV</td>
<td>0.8</td>
<td>0.7–0.9</td>
</tr>
<tr>
<td>Peak blood flow total, mL/min</td>
<td>1.0</td>
<td>1.0–1.0</td>
</tr>
<tr>
<td>Peak blood flow in basilar artery, mL/min</td>
<td>1.0</td>
<td>0.9–1.1</td>
</tr>
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</table>

CI indicates confidence interval; ICV, intracranial volume; IMT, intima-media thickness; and MRI, magnetic resonance imaging.

In the 24 patients with at least 2 cavities, 84 cavities were observed in total, 65 of which occurred together with at least one more cerebellar cortical infarct cavity within the same lobe on the ipsilateral side, whereas only 19 of these cavities occurred without a second cerebellar cortical cavity within the same lobe on the same side. Although patients with multiple cerebellar cortical infarct cavities showed a slightly higher incidence of lacunes of presumed vascular origin and a slightly lower incidence of brain stem infarcts, no significant differences were found.

**Discussion**

This study shows cerebellar cortical infarct cavities on MRI in 10% of patients with history of arterial disease. The cavities were significantly associated with age, IMT, hyperhomocysteinemia, cerebral infarcts, and intracranial atrophy, but not with WMH or white matter lacunes of presumed vascular origin. Also, they were associated with worse physical but not mental functioning.

The association with age is unsurprising as cerebellar cortical cavities are an acquired phenomenon. A previous study has shown that these cavities are surrounded by gliosis and correspond to the remnants of infarction.31 Cerebellar cortical infarct cavities were associated with markers of atherosclerosis, including high IMT and hyperhomocysteinemia.31 This suggests a large vessel origin of cerebellar cortical cavities similar to symptomatic cerebellar infarcts. As such, cerebellar cortical cavities may correspond to the chronic counterpart of small cerebellar infarctions, which have been well studied in the acute symptomatic stage of infarction. In these studies, small cerebellar infarcts were found to have the same origin as large cerebellar infarcts, most frequently being artery-to-artery and cardiogenic emboli and rarely cryptogenic.30,32 Nevertheless, small cerebellar infarcts are only rarely detected in the acute stage, except when occurring in combination with other symptomatic infarcts.11 This study now suggests that most cerebellar infarcts could be small and escape clinical attention during the acute stage of infarction.

A significant association was found between cerebellar cortical (infarct) cavities and imaging markers of cerebrovascular disease, including cortical infarcts and lacunes of ischemic origin in deep gray matter. In addition, the strong association of cerebellar cortical cavities with brain stem infarcts suggests that both may result from large vessel disease involving the same vertebrobasilar circulation territory (Figure 2). Also, the high frequency of multiple cerebellar cortical infarct cavities within the same anatomic area probably results from thromboembolic within the same perfusion territories. Although cerebellar cortical cavities were significantly associated with lacunes of presumed vascular origin in deep gray matter, this association did not hold true for lacunes in white matter. Indeed, lacunes in gray matter have been found to be merely related to atherothromboembolic closure of proximal perforating arteries, whereas lacunes in white matter more often represent small vessel disease.5,33,34 Likewise, no association was found between cerebellar cortical cavities and WMH in the cerebrum, another MRI marker of small vessel disease.35,36

Although we anticipated a relationship between cerebellar cortical (infarct) cavities and a diminished blood flow related to, for example, atherosclerotic plaques and stenosis, no association was found between cerebellar cortical cavities and total cerebral blood flow or basilar artery flow. Nevertheless, most cerebellar cortical cavities occur in the posterior lobe of the cerebellum,13 which is largely perfused by the posterior inferior cerebellar arteries arising from the vertebral arteries, the flow of which was not assessed in this study.37,38

A final interesting observation of this study was the significant association between cerebellar cortical cavities and brain atrophy, which persisted after correction for supratentorial infarcts. We hypothesize that this association could be mediated by concomitant supratentorial cerebrovascular lesions below the detection limit of 1.5-Tesla MRI, such as cerebral microinfarcts.39 Cerebral cortical microinfarcts are associated with brain atrophy in addition to cortical and subcortical macroinfarcts.40 Thus, cerebral cortical microinfarcts have shown similar associations with cerebrovascular markers on MRI as we find with cerebellar cortical cavities, which might suggest common risk factors or a shared pathophysiology of macroinfarcts, cerebral cortical microinfarcts, and cerebellar cortical infarct cavities.
Observation of cerebellar cortical infarct cavities may have the following implications. First, our study shows a significant reduction in physical functioning in patients with cerebellar cortical infarct cavities. In addition, identification of these cavities increases the visible burden of brain infarcts on MRI, and recent studies indicate that the total burden of (larger and smaller) infarcts may explain patients’ (functional) status, including cognitive performance and prognosis.1,4 Second, in daily clinical practice, cerebellar cortical infarct cavities add insights to the temporal and spatial (territorial) distribution of brain infarcts and contribute to the risk evaluation of the individual patient. In case of cerebellar cortical infarct cavities, patient’s cerebrovascular risk factors should be evaluated and optimization of preventive therapy be considered.

Strengths of our study include the large cohort of patients in which cerebellar cortical infarct cavities were meticulously studied. In addition, our cohort of patients with arterial disease presumably increased the yield of patients with cerebellar cortical infarct cavities and other manifestations of cerebrovascular diseases. Then again, most patients were included because of large vessel disease, and this could have weakened the association between cerebellar cortical infarct cavities and individual risk factors for especially large vessel disease. Another limitation is that we could not correlate cerebellar cortical infarct cavities with atrial fibrillation because of lacking data. From a technical point of view, the detection of the smallest cerebellar cortical infarct cavities (microcavities) may have been limited by the use of 1.5-Tesla MRI imaging and could have been potentially increased with the use of 3-Tesla and 7-Tesla. Nevertheless, because the cerebellar cortical infarct cavities are filled with cerebrospinal fluid, there is often a relatively large intrinsic MRI contrast between cerebrospinal fluid within the cavity and the surrounding brain tissue, which render these cavities relatively easy to detect in comparison with small infarcts with only gliosis.

In conclusion, small cerebellar cortical infarct cavities on MRI appear to be far more common than previously assumed based on symptomatic case series, and can be considered as a marker for atherothromboembolic disease of the brain.

Appendix

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Disclosures

None.

References


Cerebellar Cortical Infarct Cavities: Correlation With Risk Factors and MRI Markers of Cerebrovascular Disease
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In the article by De Cocker et al (De Cocker LJL, Kloppenborg RP, van der Graaf Y, Luijten PR, Hendrikse J, Geerlings MI; SMART Study Group. Cerebellar cortical infarct cavities: correlation with risk factors and MRI markers of cerebrovascular disease. *Stroke*. 2015;46: 3154–3160. DOI: 10.1161/STROKEAHA.115.010093.), which published online ahead of print on September 17, 2015, and appeared in the November 2015 issue of the journal, a correction was needed. The final version of the article presented regression coefficients rather than odds ratios for the functioning scales.

On page 3154, Abstract section Results, line 7, “(OR, −2.6; 95% CI, −5.7 to −0.9),” has been changed to read “(OR 0.96; 95% CI, 0.94 to 0.99).”

On page 3156, Materials and Methods Data Analysis section, second to last sentence, “Third, linear regression analysis was used to investigate whether presence of cerebellar cortical infarct cavities (independent variable) was associated with changes in physical and mental functioning (dependent variable), corrected for age and sex,” has been changed to read “Third, linear regression analysis was used to investigate whether presence of cerebellar cortical infarct cavities (dependent variable) was associated with changes in physical and mental functioning (independent variable), corrected for age and sex.”

On page 3157, fifth paragraph of the Results, “Presence of cerebellar cortical infarct cavities was significantly associated with worse physical functioning (OR, −2.6; 95% CI, −5.7 to −0.9), whereas it was not associated with mental functioning (OR, −1.1; 95% CI, −2.7 to 0.8) or MiniMental State Examination (OR, −0.4; 95% CI, −0.5 to 0.4),” has been changed to read “Presence of cerebellar cortical infarct cavities was significantly associated with worse physical functioning (OR 0.96; 95% CI, 0.94 to 0.99), whereas it was not significantly associated with mental functioning (OR 0.98; 95% CI, 0.94 to 1.02) or Mini-Mental State Examination (OR 0.97; 95% CI, 0.8 to 1.1).”

The significance of the results does not differ from the original results.

The authors regret the error.

This correction has been made to the online version of the article, which is available at http://stroke.ahajournals.org/content/46/11/3154.