Original Contribution

Cortical Microinfarcts on 3T Magnetic Resonance Imaging in Cerebral Amyloid Angiopathy

Relations With Other Magnetic Resonance Imaging Markers of Cerebral Amyloid Angiopathy and Cognition

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Background and Purpose—Cerebral microinfarcts are small ischemic lesions that are found in cerebral amyloid angiopathy (CAA) patients at autopsy. The current study aimed to detect cortical microinfarcts (CMI) on in vivo 3 Tesla (3T) magnetic resonance imaging (MRI) in CAA patients, to study the progression of CMI over a 1-year period, and to correlate CMI with markers of CAA-related vascular brain injury and cognitive functioning.

Methods—Thirty-five CAA patients (mean age, 74.2±7.6 years), 13 Alzheimer disease (AD) patients (67.0±5.8 years), and 26 healthy controls (67.2±9.5 years) participated in the study. All participants underwent a standardized clinical and neuropsychological assessment as well as 3T MRI. CMI were rated according to standardized criteria.

Results—CMI were present in significantly more CAA patients (57.1%; median number: 1, range 1–9) than in Alzheimer disease (7.7%) or in healthy controls (11.5%; $P<0.001$). Incident CMI were observed after a 1-year follow-up. CMI did not correlate with any other MRI marker of CAA nor with cognitive function.

Conclusions—In vivo CMI are a frequent finding on 3T MRI in CAA patients, and incident CMI are observable after 1-year follow-up. CMI can be regarded as a new MRI marker of CAA, potentially distinct from other well-established markers. Future larger cohort studies with longitudinal follow-up are needed to elucidate the relationship between CMI and possible causes and clinical outcomes in CAA. **(*Stroke*. 2018;49:00-00. DOI: 10.1161/STROKEAHA.118.020810.)**

Key Words: autopsy ■ cerebral amyloid angiopathy ■ cognition ■ dementia ■ magnetic resonance imaging

Cerebral amyloid angiopathy (CAA) is characterized by β-amyloid deposition in the walls of small arterioles and capillaries in the cerebral cortex and meninges.[1,2] CAA pathology is traditionally known as a cause of lobar intracerebral hemorrhages (ICH)[3,4] and microbleeds.[5] More recently, CAA has also been implicated as a cause of ischemic brain lesions[6] and neurodegeneration.[7] The mechanisms by which CAA causes neurodegeneration and impairs cognition are, however, poorly understood.

Cerebral microinfarcts are ischemic lesions of ≈50 µm–4 mm in size that have been found in the brains of CAA and dementia patients at autopsy,[8–10] and therefore might help explain cognitive dysfunction.[11–13] Recently, it was shown that cortical microinfarcts (CMI) of ≈1 to 2 mm can be detected in vivo with high-resolution 7T and 3T magnetic resonance imaging (MRI).[14] Whether CMI can be detected in vivo in CAA, and whether they relate to other markers of CAA or cause cognitive impairment is currently not known.

The present explorative study aimed to examine the frequency of in vivo CMI on 3T MRI images and their progression >1 year in a CAA cohort, and compare it with age-matched healthy controls and persons with Alzheimer disease (AD) dementia. Secondary objectives in CAA patients were to determine (1) the association of age, sex, and vascular risk factors with CMI, (2) the association between CMI and cerebrovascular reactivity and other MRI correlates of CAA, and (3) to explore relation between CMI and cognitive functioning in patients with CAA.

Materials and Methods

Anonymized data created for the study are available in a persistent repository available at http://dx.doi.org/10.5683/SP/NYR8PB.

Study Participants

This study included 40 patients with CAA that were recruited as part of the FAVR (Functional Assessment of Vascular Reactivity) study, which is an observational, prospective, follow-up study.[15] All patients

Received January 17, 2018; final revision received May 12, 2018; accepted June 1, 2018.

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met the validated modified Boston criteria for probable CAA, that require MRI evidence of lobar ICH, cerebral microbleeds, or superficial cortical siderosis without another evident cause.[3] Patients were recruited from an inpatient stroke service or an outpatient cognitive assessment clinic and presented with ICH (18 patients), transient focal neurological episodes (16 patients), or cognitive impairment (6 patients). To avoid acute effects of ICH, patients with recent symptomatic stroke (<90 days) were excluded. Patients with CAA-associated inflammation were only included if they were in remission, with resolution of acute cerebral edema. Furthermore, patients were excluded if they had abnormal visual acuity (<20/50 Snellen visual acuity), had moderate to severe dementia (Clinical Dementia Rating >1.0), or were nonfluent in English.

A group of 26 healthy controls was recruited from the community through newsletter advertisement as part of FAVR. Control participants did not have a history of stroke or dementia as examined by a neurologist and were excluded if they had silent lobar microbleeds (but not silent brain infarcts or deep microbleeds).

A total of 19 AD-dementia participants were recruited in FAVR from a memory clinic and had mild dementia (Folstein Mini-Mental Status Examination ≥20[16] and Clinical Dementia Rating[17] total score of ≤1.0). They were diagnosed by National Institute on Aging-Alzheimer's Association criteria for probable AD,[18] without biomarker support.

All study participants went through an extensive study visit, including clinical, physical, and neuropsychological assessments as well as 3T MRI. Five patients with CAA and 6 AD patients were excluded because of low-quality imaging data caused by patient motion, leaving 35 CAA patients, 13 AD patients, and 26 controls for baseline analyses. One year follow-up visits consisted of a repeated study visit and MRI. Follow-up data were available and analyzable for 21 CAA patients, 8 AD patients, and 25 controls. The follow-up imaging was done after 13.6±2.0 months. Figure 1 shows a study flow diagram, including reasons for exclusions and loss to follow-up.

All study participants provided written informed consent to participate in the study, which was approved by the Institutional Review Board of the University of Calgary. The study was conducted in adherence to the Declaration of Helsinki.

Measurements

The neuropsychological test battery was based on the battery proposed by the National Institute for Neurological Diseases and Stroke-Canadian Stroke Network.[19] Raw scores were standardized into z scores based on normative data provided by the test manuals. Z scores were then averaged in 3 domain-specific scores: memory, executive functioning, and speed of processing. The memory domain was assessed by the California Verbal Learning Test-Delayed Recall[20] and the Rey-Osterrieth Complex Figure Test-Delayed Recall.[21] The domain executive functioning included scores on the Trail Making B[22] and Controlled Oral Word Association Test-FAS.[23] Last, the domain of processing speed consisted of scores on the digit symbol coding subtest of the Wechsler Adult Intelligence Scale-IV[24] and Trail Making A.[22]

The vascular risk profile that was recorded for all patients included hypertension, diabetes mellitus, and current smoking and past smoking. This was determined by a neurologist and based on interview, medical history, and current medication use.

All imaging was performed on a 3T GE MR scanner (either Signa Excite or Discovery 750; GE Healthcare, Waukesha, WI). Because of a scanner upgrade, 5 CAA patients and 18 controls had their baseline scan on the older (Excite) system and their 1-year follow-up on the newer (Discovery) system. All other participants had both their baseline and follow-up scan on the newer system. Among other sequences, the scan protocol included T1-weighted (TR/TE/TI=6.0/2.5/650 ms; voxel size, 0.9×0.9×1 mm^3; 256×256×200_reconstructed matrix size), T2-weighted (TR/TE=3500/86 ms; voxel size, 0.9×0.9×3.5 mm^3; 256×256 matrix size), susceptibility-weighted (SWI; TR/TE=30/20 ms; voxel size, 0.5×0.5×1 mm^3; 256×256 matrix size), fluid-attenuated inversion recovery (TR/TE/TI=9000/145/2250 ms; voxel size, 0.9×0.9×3.5 mm^3; 256×256 matrix size) and T2*-weighted blood oxygen level dependent (BOLD) functional MRI (fMRI) that were acquired using a gradient-recalled echo-echo planar imaging sequence (TR/TE=2000/30 ms; voxel size, 3.75×3.75×4 mm^3; 64×64 matrix). During the fMRI acquisitions, participants passively viewed 40-second blocks of an 8-Hz contrast-reversing checkerboard, activating the primary visual cortex in the occipital lobe. These activation blocks were alternated with 40-second rest blocks of a gray screen with a central fixation cross. Blocks were repeated 4×.

MRI Rating and Analysis

CMI were rated using MeVisLab (MeVis Medical Solutions AG, Bremen, Germany; version 2.7.1), according to published autopsy-validated criteria.[25] These criteria define a CMI as a hypointense signal on the T1-weighted sequence, a hyper- or isointense signal on the fluid-attenuated inversion recovery and T2-weighted sequences <5 mm in diameter, perpendicular to the cortical surface, restricted to the cortex, and distinct from perivascular spaces (PVS).[13] After all CMI detection, corresponding locations were checked on the susceptibility-weighted imaging for susceptibility artifacts, to distinguish CMI from microbleeds. Possible CMI located in tissue affected by cortical infarcts were excluded.[25] Lobar location was assigned visually based on a template published as part of the Cerebral Haemorrhage Anatomical Rating Instrument.[26] All baseline and follow-up MR images were analyzed simultaneously by 1 trained rater (H. van den Brink). The rater was blinded to clinical participant characteristics but not scan order, because findings on baseline and follow-up were compared after initial ratings to exclude false positives (on baseline) and misses (on either baseline or follow-up). The rater could not be

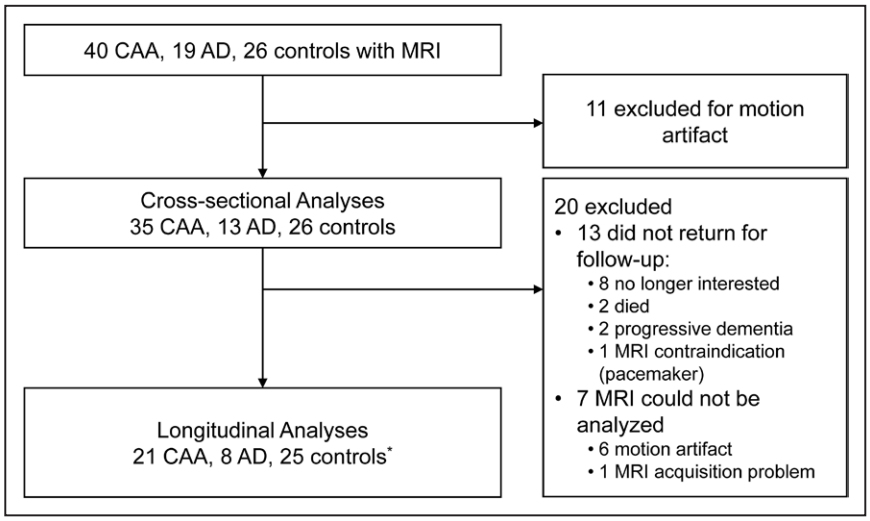

Figure 1. Flow diagram showing reasons for exclusions and loss to follow-up for participants in the study.* indicates 1 CAA excluded from analyses of new microbleeds, 5 CAA excluded from analyses of fMRI BOLD change. AD indicates Alzheimer disease; BOLD, blood oxygen level dependent; CAA, cerebral amyloid angiopathy; fMRI, functional MRI; and MRI, magnetic resonance imaging.

completely blinded for hemorrhages visible on fluid-attenuated inversion recovery or T1-weighted images, as well as microbleed load during later examination of CMI on susceptibility-weighted images. Rater H. van den Brink was trained for CMI detection on an official 3T MRI test set in the UMC Utrecht, with good reliability results on the examination scans (intraclass correlation coefficient=0.96; Dice's similarity index=0.81). Intrarater reliability was determined on a random subset of 20 images from the current study in Calgary and was good (intraclass correlation coefficient=0.87; Dice's similarity index=0.75).

Cerebral microbleeds, lacunar infarcts, large cerebral infarcts, ICH, superficial cortical siderosis, enlarged PVS, and white matter hyperintensities (WMHs) are key neuroimaging features of CAA[12] and were rated according to the STRIVE (Standards for Reporting Vascular Changes on Neuroimaging).[27] Total numbers of cerebral microbleeds, lacunar infarcts, large (>15 mm) or cortical cerebral infarcts, and ICHs were recorded. Superficial cortical siderosis was recorded as present or absent. A validated scale was used to score enlarged PVS on high-resolution T1-weighted images: 0, no PVS; 1, <10 PVS; 2, 10 to 20 PVS; 3, 21 to 40 PVS; and 4, >40 PVS.[28] WMH volumes were segmented on the fluid-attenuated inversion recovery images using Quantomo, a custom-designed software application (Cybertrials Inc; Calgary, AB, Canada).[29] To normalize for different head sizes, individual WMH volumes were analyzed as the percent of intracranial volume, where intracranial volume was obtained using FSL[30] and OptiBET.[31] Overall CAA-related small vessel disease burden was measured using a previously published scale.[32]

The change in fMRI BOLD response in the occipital cortex to a visual stimulation task was assessed as per a prior study.[33] The fMRI data were analyzed using FSL (version 5.0.1, Oxford, United Kingdom).[34]

Statistical Analyses

Baseline differences between groups were assessed with a 1-way independent ANOVA for age and Kruskal-Wallis test for MRI correlates of CAA that were non-normally distributed continuous variables. χ^2 was used to test for differences in sex, vascular risk factors, and categorical MRI variables.

CMI presence was compared between groups by a χ^2 test and differences in total numbers of CMI were tested with the Kruskal-Wallis test for both baseline counts and new CMI at follow-up. The Wilcoxon rank-sum test was used to compare total numbers of new CMI at follow-up between participants with CMI at baseline versus without CMI at baseline. Logistic regression was used to determine whether CAA status (versus controls) was associated with CMI, controlling for other differences between groups. In CAA, mean CMI counts by brain lobe were tabulated. The difference in mean CMI per lobe was tested using a generalized linear model accounting for repeated measures within the same subject. CMI numbers were weighted for lobar volume, using weights derived from the International Consortium for Brain Mapping atlas 2009c Nonlinear Symmetric[35] (frontal: 319.0 mL; parietal: 151.4 mL; temporal: 208.4 mL; occipital: 84.3 mL).

A relation of age, sex, vascular risk factors, MRI markers, and cognition to CMI was studied only in patients with CAA. Differences between patients with and without CMI were assessed with independent *t* tests for age, occipital BOLD responses, and cognitive domains; and a χ^2 test for sex and vascular risk factors. A relation of CMI with other MRI markers of CAA at baseline and follow-up were tested with χ^2 tests for categorical data and Mann-Whitney *U* tests for continuous data.

Analyses were carried out in SAS version 9.4 (Cary, NC) with the significance threshold set at $P<0.05$.

Results

At baseline, we analyzed data from 35 CAA, 13 AD, and 26 controls (Table 1). Compared with CAA, patients with AD and controls were significantly younger ($P=0.001$). Hypertension was the only other variable that occurred significantly more

Table 1. Characteristics of the Study Population

Characteristic	CAA, n=35	AD-Dementia, n=13	Control, n=26	*P* Value
Age	74.5±7.5	67.0±5.8	67.2±9.5	0.001
Sex (female)	15 (42.9)	6 (46.2)	16 (61.5)	0.34
Vascular risk factors				
Hypertension	24 (68.6)	4 (30.8)	2 (7.7)	<0.001
Diabetes mellitus	5 (14.3)	2 (15.4)	1 (3.8)	0.36
Smoking	1 (2.9)	1 (7.7)	1 (3.8)	0.75
MRI markers of CAA				
Microbleeds present	33 (94.3)	1 (7.7)	4 (15.4)	<0.001
Microbleed total	22.0 (5.0–90.0)	0 (0–0)	0 (0–0)	<0.001
Superficial siderosis	21 (61.8)	0 (0.0)	0 (0.0)	<0.001
WMH, %	1.88 (0.86–3.65)	0.36 (0.33–0.65)	0.18 (0.13–0.32)	<0.001
PVS, bg	2.0 (1–2)	1.0 (1–1)	1.5 (1–2)	0.04
PVS, cs	2.0 (1–2)	1.0 (1–1)	1.0 (1–2)	0.07
Lacunes, bg	4 (11.4)	0 (0)	1 (3.8)	0.29
Lacunes, cs	11 (31.4)	1 (7.7)	4 (15.4)	0.13
Nonlacunar infarcts	6 (17.1)	1 (7.7)	1 (3.8)	0.24

Data are presented as mean±SD, median (25th–75th percentiles), or number (percentage). WMH is expressed as the percent of intracranial volume. AD indicates Alzheimer disease; bg, basal ganglia; CAA, cerebral amyloid angiopathy; cs, centrum semiovale; MRI, magnetic resonance imaging; PVS, perivascular spaces; and WMH, white matter hyperintensity.

Table 2. Presence and Distribution of CMI in CAA and Comparison Groups

	CAA, n=35	AD-Dementia, n=13	Control, n=26	*P* Value
CMI present	20 (57.1)	1 (7.7)	3 (11.5)	<0.001
No. of CMI	1.0 (0–2.0)	0.0 (0–0)	0.0 (0–0)	<0.001
0	15	12	23	…
1	10	1	3	…
2	6	0	0	…
3	1	0	0	…
4	2	0	0	…
≥5*	1	0	0	…
Lobar count (total number in each lobe, across all patients)				
Frontal	16 (38.1)	1 (100)	2 (66.6)	…
Parietal	14 (33.3)	0 (0.0)	0 (0.0)	…
Occipital	2 (4.8)	0 (0.0)	1 (33.3)	…
Temporal	10 (23.8)	0 (0.0)	0 (0.0)	…

AD indicates Alzheimer disease; CAA, cerebral amyloid angiopathy; and CMI, cortical microinfarct.

*Fifteen CAA patient had 0 CMI, 10 had 1 CMI, etc. Other data are presented as median (25th–75th percentiles) or number (percentage).

often in patients with CAA than in AD and controls (*P*<0.001; Table 1).

CMI were present in 57.1% of patients with CAA, which was significantly more than healthy controls (11.5%) or AD-dementia (7.7%; *P*<0.001). CMI were also higher in number in CAA patients (*P*<0.001; Table 2). CMI presence and total number were not different in the different CAA presentations (ie, ICH, transient focal neurological episodes, and cognitive impairment). Nor were any of the following results different after excluding the CAA patients with cognitive impairment from the analyses. An example of a CMI in a CAA patient is shown in Figure 2. In a multivariable-adjusted model controlling for age and hypertension, CAA was independently associated with the likelihood of having CMI compared with controls (odds ratio, 7.8; 95% CI, 1.5–40.8; *P*=0.02). CMI counts in each lobe are shown in Table 2. The mean number of CMI per lobe did not differ (*P*=0.11) after taking into account differences in lobe volumes.

The characteristics of CAA patients with CMI compared with CAA patients without CMI are shown in Table 3. CAA patients with CMI did not differ in age, sex, or vascular risk factors compared with CAA patients without CMI. The presence of CMI was not associated with any of the other CAA neuroimaging markers or overall CAA small vessel disease burden. Also, baseline CMI did not predict progression of neuroimaging markers at follow-up. Cognitive domain scores did not differ between patients with CMI and patients without CMI.

In participants who had a follow-up, new CMI were identified in 9/21 with CAA (total of 16 new CMI), 1/8 with AD-dementia (total of 2 new CMI), and 0/25 controls (*P*<0.001). For 10/46 participants with CMI at baseline, 1 baseline CMI (total of 10) was not visible at follow-up. New CMI were more likely to be seen in participants with CMI at baseline (new CMI at follow-up were seen in 7/18 with CMI at baseline versus 3/36 without CMI at baseline; *P*=0.006). Follow-up scanner model (Excite versus Discovery) was not associated with new CMI detection. Compared with CAA patients without new CMI (n=12), patients with new CMI (n=9) had no evidence of different WMH progression (median, 0.44% of intracranial volume [interquartile range, −0.04% to 0.68%] versus 0.10% of intracranial volume [−0.03% to 0.45%]; *P*=0.59), frequency of new microbleeds (5/9 versus 4/11; *P*=0.39), number of new microbleeds (median, 1.0 [range, 0–87] versus 0.0 [range, 0–4]; *P*=0.13), or change in fMRI BOLD amplitude (mean, −0.02±0.70 versus −0.37±0.50; *P*=0.26).

Discussion

CMI were frequently detected on 3T MRI in CAA patients (57.1%) and significantly more than in AD patients (7.7%) and healthy controls (11.5%). After 1-year follow-up, new CMI appeared in CAA. Surprisingly, CMI in CAA did not relate with any of the other neuroimaging markers of the disease and CMI did not significantly explain cognitive dysfunction in CAA.

Our findings show that CMI are a significant new MRI marker of CAA. Moreover, compared with earlier in vivo studies, CMI seem to be much more prevalent in CAA than in healthy elderly and other patient populations. Whereas current findings show a CMI prevalence of 57.1% in CAA, earlier studies report CMI in 6.3% to 11.5% of healthy elderly,[36,37] 20% of patients with vascular cognitive impairment,[37] and

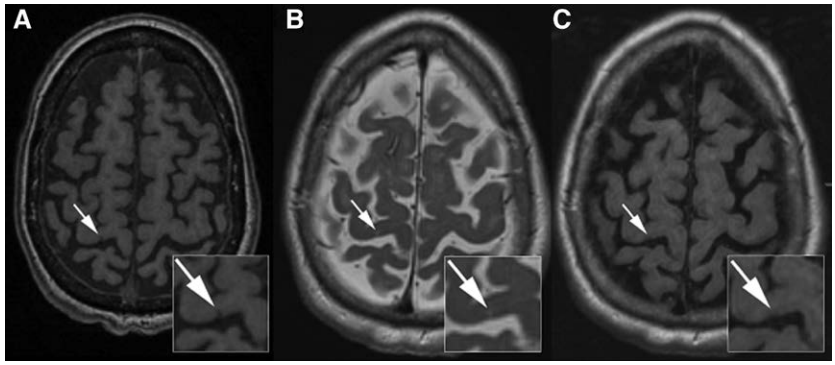

Figure 2. Example of a cortical microinfarct, seen as a hypointensity on T1-weighted (**A**), hyperintensity on T2-weighted (**B**), and isointensity on fluid-attenuated inversion recovery (**C**) image.

Table 3. Characteristics of CAA Patients With Versus Without CMI

Characteristic	CAA CMI+, n=20	CAA CMI−, n=15	*P* Value
Age	74.3±6.8	74.8±8.8	0.84
Sex (female)	8 (40.0)	7 (46.7)	0.69
Vascular risk factors			
Hypertension	15 (75.0)	9 (60.0)	0.34
Diabetes mellitus	3 (15.0)	2 (13.3)	0.89
Smoking	1 (5.0)	0 (0.0)	0.38
MRI markers of CAA			
Occipital BOLD change	1.83±0.77	2.00±0.79	0.52
Microbleeds present	19 (95.0)	14 (93.3)	0.25
Microbleed total	23.00 (6.00 to 123.00)	10.00 (5.00 to 58.00)	0.49
Superficial siderosis	10 (52.6)	11 (73.3)	0.22
WMH, %	1.75 (0.88 to 3.92)	2.05 (0.75 to 2.90)	0.63
PVS, bg	2.0 (1 to 2)	1.0 (1 to 2)	0.14
PVS, cs	2.0 (1 to 2)	1.5 (1 to 2)	0.21
Lacunes, bg	4 (20.0)	0 (0.0)	0.07
Lacunes, cs	5 (25.0)	6 (40.0)	0.34
Nonlacunar infarcts	4 (20.0)	2 (13.3)	0.60
CAA small vessel disease burden score	3.0 (2.5 to 4.0)	3.5 (2.0 to 4.0)	0.97
Progression of MRI markers			
Occipital BOLD change	−0.11±0.57	−0.61±−0.55	0.26
Number with new microbleeds	7 (50.0)	4 (44.4)	0.79
Median new microbleeds	0.50 (0.00 to 2.25)	0.00 (0.00 to 13.50)	0.82
WMH change	0.36 (0.00 to 0.61)	0.05 (−0.05 to 0.37)	0.21
Cognitive functioning			
Memory	−0.72±1.07	−0.50±0.85	0.54
Speed of processing	−1.15±1.14	−1.02±1.09	0.74
Executive functioning	−1.07±1.19	−1.21±0.96	0.71

Data are presented as mean±SD, median (25th–75th percentile), or number (percentage). WMH is expressed as the percent of intracranial volume. At baseline, 1 patient had missing microbleed and superficial siderosis information because the SWI sequence was not obtained. Three patients had missing bg PVS scores, and 4 patients had missing cs PVS scores because the scans were affected by motion. For follow-up, MRI data were available for 14 patients with baseline CMI and 9 patients without baseline CMI. AD indicates Alzheimer disease; bg, basal ganglia; BOLD, blood oxygen level dependent; CAA, cerebral amyloid angiopathy; CMI, cortical microinfarct; cs, centrum semiovale; MRI, magnetic resonance imaging; PVS, perivascular spaces; SVD, small vessel disease; SWI, susceptibility-weighted; and WMH, white matter hyperintensity.

32% of memory clinic patients.[25] Also, in our study CMI were seen significantly more often in CAA than in AD (7.7%). Residual confounding by differences in age and hypertension between CAA patients versus AD patients and controls can however not be excluded, whereas in vivo CMI detection is also limited in only capturing larger CMI.[38] Despite these limitations our prevalence is in line with neuropathological findings that report CMI in 33.3% to 87.5% of CAA patients.[8–10,39]

The much higher prevalence of in vivo CMI in CAA than in healthy elderly and other patient populations suggests that vascular β-amyloid plays a role in causing CMI. Amyloid deposition might impair normal vessel function causing decreased cerebral blood flow regulation and mismatched blood supply versus demand during brain activation. The resulting oxygen shortage might cause ischemic tissue damage, like CMI. Although we did not find that CMI were associated with fMRI BOLD reactivity, our BOLD measurement was limited to primary visual cortex, whereas the majority of CMI were found in other brain regions. In ongoing work, we are addressing this limitation by measuring vascular reactivity to carbon dioxide across the whole brain.

Interestingly, follow-up data show that in CAA a substantial number of incident CMI develop in 1 year or less. To our knowledge, our study is the first to report follow-up data on CMI detection in any condition. By showing that accumulating CMI burden can be detected with in vivo MR methods, it

becomes possible to study a causal relationship between CMI and clinical outcomes in future larger longitudinal studies. It must be noted, however, that not all baseline CMI were found at follow-up. Because intrarater reliability was good, this discrepancy is most likely caused by scan-related factors, such as different head positioning during MRI.

Even though our findings show that CMI are a marker of CAA, we did not find relationships between CMI and other key neurovascular imaging markers of CAA pathology.[12] This suggests that CMI may reflect unique pathways of CAA-related injury that are distinct from those that lead to hemorrhages, white matter changes, or perivascular space enlargement. However, given our relatively small sample size, we cannot exclude mild to moderate strength associations between CMI and other CAA markers, which merit further investigation in larger studies. Also, it must be noted that in vivo chronic CMI detection is only possible in the cortex, whereas subcortical CMI, undetectable by current imaging methods, might be more closely related to WMH. As a marker of CAA that is distinct from other markers, CMI could be a possible in vivo diagnostic aid for CAA. Although further studies, also controlling for brain atrophy, are necessary, CMI might increase diagnostic certainty when observed in the context of other well-recognized MR markers of CAA.

The main limitation of this study is the small sample size, that limited the power to study causes and consequences of CMI in CAA. This may be the reason we failed to find an association between CMI and worse cognition that has been demonstrated in non-CAA cohorts.[25,36,37,40] MRI detects only the larger CMI and thus offers only a loose approximation of the total CMI burden, which may limit the statistical power to detect associations. Also, even though rater H. van den Brink was trained extensively, the absence of interrater reliability for CMI detection in our data set poses a second limitation. Last, vascular reactivity was only studied in the visual cortex, whereas CMI were rarely found in the occipital lobe. This complicated the study of a relationship between vascular reactivity and CMI. Ongoing work addresses this limitation by measuring BOLD reactivity using carbon dioxide inhalation. This yields a measure of vascular reactivity that covers the whole brain and therefore is a better surrogate to study decreased vascular reactivity as a possible cause for CMI in CAA.

This explorative study shows that in vivo CMI are a frequent finding on 3T MRI in CAA and that incident CMI are already observed after 1-year follow-up. CMI can be regarded as a new marker of CAA pathology. Additional larger, adequately powered studies with longitudinal follow-up are warranted to determine possible causes and clinical outcomes in CAA.

Sources of Funding

The FAVR (Functional Assessment of Vascular Reactivity) study was funded by the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, and the Alzheimer Society of Canada. H. van den Brink was funded by Alzheimer Nederland, Jo Kolk Studiefonds, Hendrik Muller fonds, kfHein fonds, Stichting Korinthiers, Stichting Schuurman Schimmel-van Outeren, and Stichting Fundatie van de Vrijvrouw van Renswoude–Delft.

Disclosures

None.

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Stroke. published online July 9, 2018;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628