Intracranial atherosclerotic lesion characteristics correlate with cerebrovascular lesion load after TIA or ischemic stroke: a 7.0 tesla MRI study

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Introduction. Intracranial atherosclerosis (ICAS) is denoted as one of the most prevalent cause of stroke worldwide.[1,2] It is known that ICAS can cause different types of parenchymal injury, ranging from small lacunar infarcts to large cortical-subcortical infarcts.[3] From an ex-vivo study[4] it has been suggested that ICAS has an association with smaller (<3mm) cortical microinfarcts (CMIs) as well, but until now this was not assessed in-vivo. Moreover, from neuropathologic studies it is known that CMIs are linked to the occurrence of macroinfarcts. Given the association with macroinfarcts it has been suggested that they share a common etiology and risk factors, like ICAS.[5] Assessing both macroinfarcts and CMIs in patients with a history of cerebrovascular disease may provide additional information on the spectrum of parenchymal brain injury caused by ICAS. Therefore, in this prospective study we investigated the presence of CMIs at 7.0 tesla (7T) MRI in patients with a transient ischemic attack (TIA) or ischemic stroke of the anterior circulation and explored the relationship between ICAS, CMIs and macroinfarcts.

Materials and Methods. Institutional Review Board approval was obtained for this prospective study. All patients gave written informed consent. Patients presenting with arterial ischemic stroke or TIA of the anterior cerebral circulation were screened for inclusion in this study. Imaging was performed on a whole body 7T MR system (Philips Healthcare, Cleveland, OH, USA) with a 32-channel receive coil and volume transmit/receive coil for transmission (Nova Medical, Wilmington, MA, USA). The protocol included a T_1-weighted Magnetization Preparation Inversion Recovery Turbo Spin Echo (MPIR-TSE)[6] intracranial vessel wall sequence (acquired resolution 0.8x0.8x0.8mm^3, repetition time (TR) 3952ms, inversion time (TI) 1375ms, echo time (TE) 37ms, scan duration 11min) before and in 15 cases also after contrast administration, and a T_2-weighted Fluid-Attenuated Inversion Recovery (FLAIR) sequence (acquired resolution 0.8x0.8x0.8mm^3, TR/TE/TI 8000/300/2250ms, scan duration 13min) after contrast administration. Five minutes before acquisition of the contrast enhanced MPIR-TSE sequence, 0.1 mL/kg of a gadolinium-containing contrast agent (Gadobutrol, Gadovist 1.0 mmol/mL, Bayer Schering Pharma, Newbury, UK) was administered to the patients. Image analysis was performed with MeVisLab v2.5 (MeVis Medical Solutions AG, Bremen, Germany) and on an offline workstation (Philips). ICAS lesions, characteristics of ICAS lesions (concentric/eccentric; focal/diffuse, enhancement[7]), and ischemic lesions (CMIs and macroinfarcts) were scored by two independent raters (ND and AK) (Figure 1). The Intraclass Correlation Coefficient (ICC) and the Dice Similarity Coefficient (DSC) were evaluated for interrater reproducibility. Consensus was reached for every location. SPSS version 20 for Windows was used for statistical analysis. First, the relation between ICAS lesions, infarcts (macroinfarcts and CMIs), and baseline characteristics were examined using logistic and linear regression analyses, where appropriate. Second, linear regression analyses were used to examine relationships between calculated ratios of ICAS lesion characteristics, CMIs and macroinfarcts. Statistical significance was set at $p<0.05$ and standardized Beta coefficients are given where appropriate.

Results. Between Augustus 2011 and March 2014, nineteen patients (6 females; mean age 59 years; range 40-81 years) with a TIA (n=7) or ischemic stroke (n=12) of the anterior circulation, who fulfilled the inclusion criteria, underwent 7T imaging at a median time of 5 days after symptom onset (range 1-10 days). One patient was excluded because of poor image quality, due to motion artifacts. A total number of 101 CMIs (in 78% of patients), 31 macroinfarcts (67%) and 75 ICAS lesions (100%) were found. Eighty-one and sixty-five percent of the CMIs and macroinfarcts, respectively, were found in the same vascular territory as the ICAS lesions. A strong interrater reliability was found for both CMIs (ICC: 0.95), macroinfarcts (ICC: 0.81) and ICAS (ICC: 0.75). Interrater agreement on the evaluation of locations was good to strong (DSC for CMIs, macroinfarcts and ICAS were 0.66, 0.75 and 0.70, respectively). Age and gender were not related to vascular lesion load (macroinfarcts and CMIs) and the number of ICAS lesions did not have a relationship with the vascular lesion load either. A positive correlation existed between the number of macroinfarcts and CMIs ($\beta=0.538$, $p<0.05$); furthermore, macroinfarcts were positively correlated ($p<0.05$) to history of stroke, but CMIs and ICAS lesions were not. When examining correlations between ICAS lesion characteristics and infarcts a positive correlation was found ($\beta=0.690$, $p<0.01$) for a concentric configuration and macroinfarcts, but not for CMIs. A diffuse thickening pattern was positively correlated to macroinfarcts ($\beta=0.510$, $p<0.05$) and a weak trend was found for CMIs ($\beta=0.407$, $p=0.09$). Enhancement did not have any relationship with cerebrovascular lesion load.

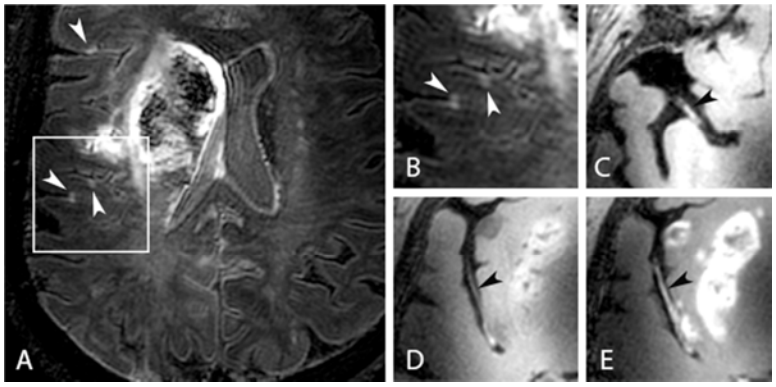

Figure 1. A 75-year-old female patient presented with ischemic stroke of the right middle cerebral artery (MCA) territory. (A) Transverse 7T T_2-weighted Fluid-Attenuated Inversion Recovery image shows an infarct of the right MCA territory and three cortical microinfarcts (**white arrowheads**); B shows a zoomed view of the box drawn in A. (C-E) Transverse 7T T_1-weighted magnetization preparation inversion recovery turbo spin echo images before (C and D) and after contrast administration (E) show thickening of the right M1 (C) and M2 (D) segments of the MCA, and enhancement of the M2 vessel wall segment after contrast administration (E) (**black arrowheads**).

Conclusion. This study shows that in patients with TIA and ischemic stroke CMIs represent a relevant portion of the total cerebrovascular lesion load and coexist with macroinfarcts. Although CMIs were only shown to have weak correlations with specific ICAS characteristics it may well be that larger studies will demonstrate that ICAS is a shared etiology between macroinfarcts and CMIs. These results shine new light on the spectrum of parenchymal damage caused by ICAS.

References. [1]Arenillas et al., Stroke, 2011; [2]Qureshi et al., Lancet, 2013; [3]Adams et al., Stroke, 1993; [4]Zheng et al., Stroke, 2013; [5]Longstreth et al., Alzheimer Dis Assoc Discord, 2009; [6]van der Kolk et al., Stroke, 2011; [7]Dieleman et al., Neurology, 2014