Total cerebral blood flow studies in CADASIL

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Introduction
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an increasingly recognised disorder that is based on mutations of the notch 3 gene leading to migraine, transient ischemic attacks and early onset of lacunar stroke with dementia. A hallmark of CADASIL is the presence of areas with increased signal intensity on T2-weighted MR images in the white matter[1]. The exact pathogenesis of these white matter abnormalities remains poorly understood. Chronic ischemia due to structural changes of the arterial wall is presumed to cause these tissue lesions.

It has been shown that diminished cerebral blood flow and/or cerebrovascular reactivity (CVR) are related to the presence of cerebral white matter hyperintensities in the elderly[2-3]. In CADASIL, it is relatively unexplored which of these functional parameters leads to white matter lesions.

One method to assess total cerebral blood flow (TCBF) is quantitated flow mapping (QF) using phase contrast MR[4]. Using QF, the CVR can be estimated by measuring the flow in both internal carotid arteries and the basilar artery, before and after the administration of a vasodilating agent such as acetazolamide (ACZ). This method is robust, easy to perform, and permits straightforward quantification.

The aim of this study is to investigate whether global changes in cerebral blood flow are present in CADASIL patients by assessing the baseline TCBF, the maximum TCBF after administration of ACZ and CVR.

Methods
We performed baseline flow measurements in 30 patients (mean age 44 years, range 21-60) with proven CADASIL and in 30 age and sex matched healthy volunteers. In 18 of these patients (mean age 45 years, range 22-58) TCBF was measured after administration of ACZ. 18 healthy volunteers were used as control subjects (age and sex matched). Clinically, the group CADASIL patients included symptomatic as well as asymptomatic patients.

All imaging was performed on a 1.5T MR system (Philips Medical Systems, Best, The Netherlands). For flow measurements we used a non-triggered gradient echo phase contrast technique (TR/TE 16/9ms; flip angle 7.5°; 5 mm slice thickness; FOV 250mm with eight NSA). The scans were performed in a plane perpendicular to the left and right internal carotid artery and the basilar artery. Images were analysed using the locally developed software package FLOW® (Department of Radiology; Division of Imaging Processing, LUMC).

The TCBF was measured before and 20 minutes after the administration of 14 mg/kg ACZ iv. The baseline TCBF and the maximum TCBF were respectively defined as flow before and 20 minutes after administration of ACZ. CVR was defined as percentage change in baseline TCBF and its clinical relevance.

Results
ACZ significantly increased TCBF in the patient as well as in the control group (p<0.01). In CADASIL, the baseline TCBF and maximum TCBF were significantly decreased (p<0.01) compared with the control values (552 ± 128 vs. 671 ± 127 ml/min and 890 ± 231 vs. 1117 ± 208 ml/min). No significant difference of the CVR (37% vs. 40%) was found between the two groups.

Discussion
This is the first study on global cerebral blood flow in CADASIL patients. We found a reduction in baseline TCBF and maximal TCBF, but not in CVR in CADASIL patients. This suggests that reduction in the diameter of blood vessels is responsible for ischemic alterations in the brain and not the reduction of the vasoreactivity of the vessels. These results are in contrast with the reduction of CVR reported in a study performed with MRI bolus tracking[5]. This discrepancy might be related to the heterogeneity of our population (age range 21-60 years, symptomatic as well as asymptomatic patients) and a different technique to assess TCBF[6]. QF has several advantages over perfusion MR. It is easier to perform, it is more straightforward to quantify, and the reproducibility is better than perfusion imaging[7]. Future studies are necessary to investigate the association between white matter lesions and reduction of the TCBF and its clinical relevance.

References