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ORIGINAL ARTICLE

Is there an association between leukoaraiosis volume and diabetes?

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KEYWORDS
Leukoaraiosis;
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Summary
Objectives: The relation between white matter loss (WML) and diabetes is still debated. The aim of this study was to investigate the correlation between typical WML— and diabetes-related magnetic resonance imaging (MRI) findings in a cohort of patients scheduled for carotid endarterectomy (CEA).
Materials and methods: Ninety-three consecutive patients (mean age 71 ± 9 years; male 71) were included in a single-centre retrospective study. All the patients underwent MRI as baseline evaluation prior to CEA. A neuroradiologist blinded to the presence of risk factors calculated WML volume and number of lesions on FLAIR images using a semi-automated segmentation technique. Receiver operating characteristics analysis was performed to search for any association between WML volume and the number of WML lesions. The Mann—Whitney tests were used to determine significant WML differences between diabetic and non-diabetic patients. Logistic regression analysis was performed to evaluate the potential association of other variables.
Results: The prevalence of diabetes was 20.4% ($n = 19$). WML volume and number of WML lesions were significantly associated with diabetes ($P = 0.001$). A statistically significant difference in WML volume was found between diabetic and non-diabetic patients ($P < 0.0001$). Only diabetes, among all the investigated variables (WML volume, CAD status, age, smoking status, gender, hypertension, hyperlipidemia, diabetes) was significantly associated with WML ($P = 0.0001$).

Abbreviations: MRI, Magnetic resonance imaging; WML, White matter loss; CAD, Coronary artery disease; CEA, Carotid endarterectomy; ROC, Receiver operating characteristics; AUC, Area under the curve; DWI, Diffusion weighted imaging.

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Conclusion: Our results demonstrate a strong statistical correlation between diabetes and WML. Future scientific challenges could include the identification of potential therapeutic targets and the creation of dedicated screening protocols for WML in diabetic patients other than the simple measurement of leukoaraiosis total burden.

Introduction

Leukoaraiosis (LA) is a term coined by Hachinsky et al. [1] back in 1986 to define a diminution of representation of the white matter density; currently LA refers to the identification of areas of high signal intensities on T2-weighted and proton density sequences at magnetic resonance imaging (MRI), representing regions of scattered brain white matter loss (WML) associated with local increase in brain water content [2].

Despite numerous multi-centric studies published on the topic, the exact incidence of LA in the elder population remains unknown with current estimates varying greatly (5.3—95%) [3—5]. The cause of WML is not clear; it is probably related to low-grade vascular insufficiency (e.g. hypo-perfusion, arteriolar disease) leading to an atrophic perivascular demyelinization (corresponding to the histopathological findings of ischemic demyelinization and gliosis) [6]. Several studies have investigated the relationships between WML and various factors, including carotid plaque, age, stroke, hypertension, disability, cognitive decline, depression, gait and urinary disturbances [7—9]. Despite the supposed vascular etiology of WML, the precise relation with diabetes is still debated, since several authors reported quite discordant results on this association. Tiehuis et al. demonstrated that diabetic patients had more global and subcortical brain atrophy and larger WML lesions than matched non-diabetic patients [10]. Khan et al. confirmed a strong correlation between LA and diabetes in a large patient cohort [11]. On the contrary, other studies have not confirmed this association. Bogousslavsky et al. suggested that WML lesions are clearly correlated with hypertension, but not with diabetes [12]; van Harten et al. reported no association between diabetes and WML (OR 1.1 [95% CI 0.9—1.4]) in a cohort of patients with stroke or other cardiovascular risk factors and a mild association in the outpatient population [13]. The aim of the present study was to evaluate the association between diabetes and WML in a cohort of patients who underwent brain MRIs at our institution, in order to add further information to the current knowledge on the topic.

Materials and methods

Demography

Because of the retrospective nature of the study, the requirement for written informed consent was waived. Our cohort was composed of ninety-three consecutive patients (mean age 71 ± 9 years; male 71) scheduled for carotid endarterectomy (CEA) according to the NASCET and SPREAD guidelines [14—16]. Brain MRI was performed in all the patients as baseline evaluation before surgery. In this cohort of patients, only 32 were symptomatic (presenting with a history of transient ischemic attack or stroke or any neurological deficit occurring at least one month earlier) [16]. Considering the vascular risk factors, information about hypertension, diabetes, hyperlipidemia, previous medical history of coronary artery disease (CAD), and smoking habits were recorded for the entire study population. The evaluation of risk factors was performed in accordance with international guidelines, on the basis of clinical data and laboratory tests performed at baseline and/or considering previous medical records in patients on pharmacological treatment. Hypertension was defined as a blood pressure persistently at or above 140/90 mmHg. Diabetes was defined based on clinical history of two fasting glucose measurements above 126 mg/dL (7.0 mmol/L). Hyperlipidemia was defined as elevated plasma concentrations of any or all of the lipids.

We considered as exclusion criteria:

- other possible etiology for white matter disease, such as vasculitis, demyelinating disease and connective tissue diseases;
- previous pathologies, such as abscess, encephalitis or brain malignancy.

Brain MRI protocol and lesion assessment

Brain MRI examinations were performed using a Gyroscan 1.5-T superconducting magnet (Philips, Best, The Netherlands), with a head coil according to a standardized protocol. In each patient diffusion weighted imaging (DWI) was performed with a single-shot spin echo sequence with two diffusion-sensitivity values of 0 and 1000 s/mm^2 along the transverse axis. In addition to DWI sequences, axial and sagittal 2D FLAIR images (10,000/140/220 ms for TR/TE/TI; matrix 512 × 512; FOV: 240 × 240 mm^2; section thickness: 5 mm) were also obtained.

WML was identified from axial and sagittal FLAIR images by a neuroradiologist with 12 years of experience, blinded to the presence of risk factors; once the neuroradiologist identified the lesions, WML volume was automatically calculated using a semi-automated segmentation technique (Jim, Xinapse System, Leicester, UK). WML was defined as any hyperintense white matter region on FLAIR images not related to large vessel infarcts (Fig. 1). After the delineation of WML, its volume for each hemisphere, including both periventricular and deep subcortical lesions, was automatically calculated by the software, based on the slice thickness and outlined WML areas.