



## Ischemic cerebrovascular burden evaluated by magnetic resonance imaging in an elderly Brazilian community: The Pietà study



Elisa de Paula França Resende <sup>a</sup>, Luciana Costa-Silva <sup>a</sup>, Karoline Carvalho Carmona <sup>a</sup>, Thais Helena Machado <sup>a</sup>, João Carlos Barbosa Machado <sup>b</sup>, Henrique Cerqueira Guimarães <sup>a</sup>, Maira Tonidandel Barbosa <sup>a</sup>, Antônio Lúcio Teixeira <sup>a</sup>, Leonardo Cruz de Souza <sup>a</sup>, Paulo Caramelli <sup>a,\*</sup>

<sup>a</sup> Faculdade de Medicina da Universidade Federal de Minas Gerais, Av. Prof Alfredo Balena, 190, room 246, Belo Horizonte, MG 30130-100, Brazil

<sup>b</sup> Faculdade de Ciências Médicas de Minas Gerais, Alameda Ezequiel Dias, 275, Belo Horizonte, MG 30130-110, Brazil

### ARTICLE INFO

#### Article history:

Received 24 May 2016

Received in revised form 8 August 2016

Accepted 28 November 2016

Available online 1 December 2016

#### Keywords:

White matter lesions

Aging

Dementia

Hypertension

### ABSTRACT

In developing countries, cardiovascular risk factors are poorly controlled, leading to high prevalence of cerebrovascular diseases. The aim of the study was to evaluate the burden of white matter lesions in magnetic resonance through the Fazekas scale in a population aged 75+ years living in the community, and to investigate possible associations between vascular lesions, cardiovascular risk factors and cognitive status. Subjects were selected from a community-based study on brain aging conducted in Caeté (Minas Gerais state), Brazil. Overall, 177 participants (112 cognitively healthy, 36 with cognitive impairment-no dementia and 29 with dementia), being 108 women, aged  $79.3 \pm 3.8$  years, with  $3.1 \pm 2.9$  years of educational level, underwent a 3 Tesla magnetic resonance scanner with fluid attenuated image recovery acquisition. Severity of white matter lesions was assessed through the Fazekas scale. Severe white matter lesions were present in 31.1% of the whole sample and in 25.0% of the cognitively healthy individuals. A significant association was found between severe white matter lesions and cognitive impairment (OR = 2.20, 95% CI 1.17–6.53;  $p = 0.021$ ), as well as with hypertension (OR = 1.92, 95% CI 1.03–7.39;  $p = 0.043$ ). In conclusion, a high prevalence of severe white matter lesions was observed in this elderly Brazilian population sample, and white matter lesions were associated with hypertension and cognitive status. Importantly, the prevalence of white matter lesions was also high in cognitively healthy subjects.

© 2016 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### 1. Introduction

Aging and brain vascular disease share reciprocal relationships: on one side, cerebral small vessel disease (SVD) is a common finding in aging; on the other hand, aging is a risk factor for cerebral SVD [1]. Such changes appear as white matter hyperintensities (WMH) on T2 weighted magnetic resonance imaging (MRI) and are called leukoaraiosis when detected by computed tomography. The clinical meaning of these findings is a matter of debate as cerebral SVD can be related either to pathological conditions, such as stroke or cognitive decline, or can be observed in asymptomatic individuals [2]. Whilst cerebral SVD is considered the most common cause of vascular dementia [3], it also frequently coexists with neurodegenerative disorders,

sharing risk factors with Alzheimer's disease (AD) [4], and constitutes an important determinant of age-associated functional impairment [5].

As defined by an international consensus, MRI-visible WMH are markers of cerebrovascular disease [6] and are considered imaging-based biomarkers of vascular lesions [7,8]. Studies have shown that their pathologic correlates are arteriosclerosis [9] and its consequences, vasogenic edema [10] and cerebral amyloid angiopathy [11].

Studies from developed countries have shown that prevalence of cerebral SVD, as assessed by MRI, is high. For instance, in a North-American study the overall prevalence of white matter lesions was 15.8%, increasing from 7.9% in the 55 to 59 year-old age group to 22.9% in the 65 to 72-year-old age group [12]. In United Kingdom, the prevalence of white matter lesions assessed by post-mortem MRI in the elderly was 94% [13]. In Latin America, a histopathological study showed that 16.8% of cognitively healthy individuals had cerebral SVD. Furthermore, cerebral SVD was significantly associated with different causes of dementia: AD, vascular dementia and mixed dementia [14,15].

Elderly inhabitants from developing countries usually have on average low educational levels, which might compromise access to better health care services and to a healthier life style. Therefore, these populations are exposed to poor control of cardiovascular risk factors, and

Abbreviations: AD, Alzheimer's disease; CIND, cognitive impairment-no dementia; FAQ, Functional Activity Questionnaire; FLAIR, fluid attenuated inversion recovery; MRI, magnetic resonance imaging; MMSE, Mini-Mental Status Examination; SVD, small vessel disease; WMH, white matter hyperintensities.

\* Corresponding author at: Av. Prof Alfredo Balena, 190 room 246, 30130-100 Belo Horizonte, MG, Brazil.

E-mail address: [caramelli@ufmg.br](mailto:caramelli@ufmg.br) (P. Caramelli).

display an elevated prevalence of cerebrovascular disease [14]. In addition, there is convincing evidence from the Brazilian brain bank of the Brazilian Aging Study indicating that even a few years of education, when compared to illiteracy, provide resilience against neuropathological burden, in accordance with the cognitive reserve hypothesis [16]. Therefore, the combined large burden of cardiovascular disorders and lower cognitive reserve background suggests that cerebrovascular disease may play a major role in cognitive decline and dementia in developing countries [17]. Accordingly, recent results from the long-term follow-up of the Framingham cohort have shown a suggestive decline in dementia incidence across a three decade span, especially in highly educated participants, which is supposed to be associated with a better control of cardiovascular risk factors or conditions [18,19].

Previous studies assessed the prevalence of cerebral SVD in developed countries, but very few focused on individuals older than 75 years. One study in Europe reported WMH in 68.2% of subjects aged 75 + years [20], while another described the presence of severe lesions in 50% of those aged 85 + years [21]. As far as we are aware, no previous study in Latin America evaluated cerebral SVD in a community setting using MRI. In the present study we investigated WMH burden assessed through MRI in a community-based sample of individuals aged 75 + years with low educational level. We hypothesized that prevalence of cerebral SVD would be high in this population regardless of reported symptoms, and its' severity would be associated with cognitive impairment.

## 2. Methods

### 2.1. Population

The participants were selected from the Pietà study, a community-based investigation on brain aging conducted in Caeté (Minas Gerais state), Southeast of Brazil [22]. Elderly individuals aged 75 + years, targeted in this study, were 1251 (3.2% of the total population) according to the Brazilian Institute of Geographic and Statistics [23]. They were actively searched through community-health program agents from the local government; announcements on local radios and newspapers were also strategically posted. As for institutionalized elderly, the research team visited the two existing long-term care institutions in the town. Overall, 639 individuals, corresponding to 51.1% of the city population aged 75 + years were evaluated. Participants were submitted to a thorough clinical, neurological and functional evaluation. Blood samples were collected for routine laboratory tests, including TSH, B12 vitamin and VDRL to rule out reversible causes of cognitive impairment. The clinical, functional, neurological and psychiatric status of the participants was established according to the performance on the cognitive tests and on careful group discussions and consensus agreement among the examining physicians. Participants were submitted to the Mini-Mental Status Examination MMSE [24,25] and to a Brief Cognitive Screening Battery [26]. Functional performance was assessed with the Functional Activity Questionnaire (FAQ) [27]. Individuals were considered to be cognitively efficient when they had a performance in the MMSE and in the Brief Cognitive Battery above the 25th percentile according to age and educational level, in agreement with previous Brazilian reports [28–31]. A cut-off of 5 points on the FAQ was set to define a significant level of functional impairment [32]. For the purpose of the present study, the participants were classified into cognitively healthy when they had the expected performance for age and education in the tests and no functional impairment. When there was cognitive impairment, but functional independence (FAQ  $\leq$  5), they were classified as cognitive impairment-no dementia (CIND) [33,34]. As this was a population-based study, the CIND concept [35] was preferred instead of mild cognitive impairment (MCI) because it is a broader concept and it is not necessarily associated with cognitive complaint. This latter feature is particularly relevant given the sociodemographic profile of the study population (advanced age and low schooling). Indeed, most CIND

subjects and/or their relatives did not have cognitive complaints, and cognitive impairment was identified only after clinical and neuropsychological evaluation. Finally, the diagnosis of dementia was made based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition criteria [36].

Antecedents of myocardial infarction and dyslipidemia were assessed with a standardized medical questionnaire administered to the individuals or to their relatives, whenever necessary. Diabetes mellitus was considered to be present if the subject had a previous diagnosis and/or was taking oral antidiabetics or insulin. Blood pressure was measured in the sitting position at the right upper arm with a random-zero sphygmomanometer. A subject was considered to have hypertension if he/she provided a compatible medical history of hypertension or when he/she was taking antihypertensive drugs.

### 2.2. Standard protocol approvals, registrations, and patient consents

This study was approved by the Ethics Committee of the Federal University of Minas Gerais. All participants or their legally acceptable representatives signed the written informed consent.

### 2.3. Neuroimaging data acquisition, processing and analysis

A random subsample of the individuals from the Pietà study ( $n = 200$ ) was asked to take part in the MRI examination. The effective sample used in this study ( $n = 177$ ) included participants with acceptable quality of the fluid attenuated inversion recovery (FLAIR) images acquired in a 3 Tesla Philips Achieva scanner. The FLAIR images were obtained in axial plane with a single-shot, spin-echo echoplanar sequences in the axial plane (TR/TE = 10,000/140 ms, Inversion time: 2800 ms, Echo train length: 27 mm, FOV = 240 mm, matrix = 352  $\times$  212 (reconstructed 512  $\times$  512), slice thickness = 5.0 mm with 0.5 mm gap between slices).

An experienced radiologist (LCS), blind to all clinical information, centrally performed the assessment of the severity of WMH on axial FLAIR images using the Fazekas scale. The Fazekas score is rated according to the presence of WMH in FLAIR images: zero refers to no white matter lesions (including symmetrical, well-defined caps or bands), one refers to the presence of focal lesions, two refers to the presence of beginning confluent lesions, and three refers to the presence of diffuse involvement of the entire white matter, with or without involvement of U fiber [37,38]. Deep and periventricular white matter were separately considered for the analysis. Brainstem hyperintensities were excluded. This scale does not evaluate acute vascular lesions or lacunes. According to WMH severity, patients were subdivided into three groups: absent/mild changes (Fazekas 0 and 1), moderate changes (Fazekas 2) and severe changes (Fazekas 3) [37].

### 2.4. Statistical analysis

Absolute frequencies of different levels of WMH were measured as total numbers of mild intensity (Fazekas 0 and 1), moderate intensity (Fazekas 2), and severe intensity (Fazekas 3). The frequencies were also divided by sex, age and cognitive status: cognitively healthy, CIND and dementia. Age was divided into three groups: 75 to 79, 80 to 84 and 85 and older. Koromogov-Smirnov test was used to check the normality of the sample. The chi-square test or Fisher's exact test, when appropriate, was used for categorical variables. Kruskal-Wallis test was used for quantitative variables.

Logistic regression analysis was employed to evaluate the association between severe WMH group and the following variables: cognitive impairment (dementia and CIND), history of myocardial infarction, hypertension, diabetes and dyslipidemia, adjusted for age, sex, and schooling. SPSS (version 22; Statistical Package for the Social Sciences, Chicago, IL) was employed, and the value of significance was accepted as a  $p$ -value  $< 0.05$  in two-tailed tests.

Download English Version:

<https://daneshyari.com/en/article/8683460>

Download Persian Version:

<https://daneshyari.com/article/8683460>

[Daneshyari.com](https://daneshyari.com)