European Journal of Radiology 89 (2017) 111–116

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Original research

Relationship between white matter hyperintensities volume and the circle of Willis configurations in patients with carotid artery pathology

Luca Saba [a,*], Roberto Sanfilippo [b], Michele Porcu [a], Pierleone Lucatelli [c], Roberto Montisci [b], Fulvio Zaccagna [c], Jasjit S. Suri [d,e,f], Michele Anzidei [c], Max Wintermark [g]

[a] Department of Radiology, Azienda Ospedaliero Universitaria (A.O.U.), di Cagliari – Polo di Monserrato, s.s. 554 Monserrato, Cagliari 09045, Italy
[b] Department of Vascular Surgery, Azienda Ospedaliero Universitaria (A.O.U.), di Cagliari – Polo di Monserrato, s.s. 554 Monserrato, Cagliari 09045, Italy
[c] Department of Radiology, University la Sapienza, Rome, Italy
[d] Monitoring and Diagnostic Division, AtheroPoint™, Roseville, CA, USA
[e] Point-of-Care Devices, Global Biomedical Technologies, Inc., Roseville, CA, USA
[f] Department of Electrical Engineering, University of Idaho (Affl.), ID, USA
[g] Department of Radiology, Stanford University, USA

ARTICLE INFO

Article history:
Received 17 November 2016
Received in revised form 17 January 2017
Accepted 30 January 2017

Keywords:
White matter hyperintensities
Circle of Willis
Carotid artery pathology

ABSTRACT

Purpose: We aimed to assess if there is a difference of distribution and volume of white matter hyperintensities (WMH) in the brain according to the Circle of Willis (CoW) configuration in patients with carotid artery pathology.
Material and methods: One-hundred consecutive patients (79 males, 21 females; mean age 70 years; age range 46–84 years) that underwent brain MRI before carotid endarterectomy (CEA) were included. FLAIR-WMH lesion volume was performed using a semi-automated segmentation technique and the status of the circle of Willis was assessed by two neuroradiologists in consensus.
Results: We found a prevalence of 55% of variants in the CoW configuration; 22 cases had one variants (40%); 25 cases had two variants (45.45%) and 8 cases showed 3 variants (14.55%). The configuration that was associated with the biggest WMH volume and number of lesions was the A1 + PcoA + PcoA. The PcoA variants were the most prevalent and there was no statistically significant difference in number of lesions and WMH for each vascular territory assessed and the same results were found for AcoA and A1 variants.
Conclusion: Results of our study suggest that the more common CoW variants are not associated with the presence of an increased WMH or number of lesions whereas uncommon configurations, in particular when 2 or more segment are missing increase the WMH volume and number of lesions. The WHM volume of the MCA territory seems to be more affected by the CoW configuration.

1. Introduction

Among vascular risk factors, white matter hyperintensities (WMH) are strongly associated with age, hypertension and diabetes [1,2], but they have also been associated with dementia, gait abnormalities, and depression [3,4]. Moreover, some authors proved that WMH is an independent risk factor for stroke [5]. Pathologic findings in subjects with WMH include alteration of myelin, astrocytic gliosis and axonal loss [6,7].

Ninety percent of subjects aged 80 years and older exhibit some degree of white matter changes [8,9]. The pathogenesis of WMH is not clear and it is believed that those hyperintensities result mostly from small-vessel disease [10,11]. Nevertheless, several papers demonstrated a correlation between large-vessel disease, i.e. internal carotid arteries stenosis and plaque's features, and WMH [12–14].

The circle of Willis (CoW) was first described in 1664 [15] and represents an exceptional circulatory anastomosis between the carotid arteries and the vertebra-basilar system. Prevalence of WMH is increased in subjects with an incomplete CoW compared with those with a full CoW configuration [16]; proving that the insufficient collateral blood flow increases the subcortical white matter's vulnerability to hypotension-induced low flow effects [17]. Indeed, whilst some authors confirmed an increase in disease burden in the presence of an incomplete CoW; others suggested

* Corresponding author.
E-mail address: lucasaba@tiscali.it (L. Saba).

http://dx.doi.org/10.1016/j.ejrad.2017.01.031
0720-048X/

no association or, even, a potential protective effect of some CoW's variants [18–21].

Therefore, the purpose of this study was to assess the relationship between the volume and distribution of WMH and the circle of Willis' configuration in patients with carotid artery disease, by assessing the effect of the different variants to the WMH in the different arterial territories (ACA, MCA and PCA) and to the periventricular white matter (PVWM) and deep white matter (DWM).

2. Material and methods

2.1. Study design and patient population

This is a retrospective study. The Institutional Review Board approval was obtained and patient's consent was waived because of the retrospective category. Based on a power calculation we estimated that a sample size of 90 patients would yield a 96% power to detect a 10% difference in WMH volume among the different CoW configuration at the 5% significance level. We decided to include also a correction of 10% and, therefore, the sample size was set at 100 subjects.

The internal database was searched to identify potential patients who underwent a brain MRI before CEA. In our Hospital subjects were treated with CEA according to the recommendations by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [27], the Stroke Prevention and Educational Awareness Diffusion (SPREAD) [28] and European Carotid Surgery Trial (ECST) [29] after the exclusion of cardio-embolic source of embolism performed with echocardiography.

Because WMH is strongly associated with the age, we included patients aged more than 40 years in order to avoid confounding factors age-related. We opted for the following exclusion criteria:

(1) Stroke due to large vessel occlusion (subjects with lacunar strokes were included). Moreover, patients with stroke due to cardiac embolism were not included because they were not candidate to CEA procedure.
(2) Other pathologies that can determine white matter diseases (vasculitis, demyelinating diseases, connective tissue diseases);
(3) Other brain's pathologies (neoplasms, abscesses, encephalitis).

Subjects with transitory ischemic attack (TIA) with the absence of stroke imaging related to the occlusion of large vessel were included in the study. Using those criteria, we included in this study 100 consecutive patients that underwent brain MRI in our Hospital form March 2012 to October 2014 (79 males, 21 females; mean age 70 years; SD 8 years; age range 46–84 years). A subgroup of patients has been already included in previously published studies [21].

2.2. MR imaging technique

Brain MR examinations were performed according to a previously described technique using a 1.5-T MRI scanner (Gyroscan, Philips, Best, The Netherlands) and a 16 channel head coil [**Blinded for peer review**]. As part of our general brain protocol, axial and sagittal 2D FLAIR images (10000/140/2200 msec for TR/TE/TI; matrix: 512 × 512; FOV: 240 × 240 mm) were obtained and used for the determination of WMH volume.

We include also (a) an axial single-shot spin-echo Diffusion weighted imaging (DWI) sequence with two b values (0 and 1000 s/mm^2); (b) an axial spin-echo T1-weighted sequence (500–600/15/2 for TR/TE/excitations) with a flip angle of 30°; matrix, 512 × 512; FOV 240 mm^2, section thickness of 5 mm; (c) an axial fast spin-echo T2-weighted images (2200- 3200/80-120/1.2 for TR/TE/excitations); turbo factor, matrix, 512 × 512; FOV, 240 mm^2; section thickness, 5 mm; (d) an axial 2D T2*-weighted gradient echo (TR shortest; TE 23 ms); flip angle 15°; in-plane resolution 0.9 × 0.9 mm; FOV 230 mm^2; matrix 512 × 512; slice thickness 5 mm.

In all patients, a three-dimensional (3D) multislab time of flight (TOF) MRA of the CoW was performed [**Blinded for peer review**]. The volume of interest included from the petrous portion of the internal carotid artery to the level of the genu portion of the corpus callosum. The following parameters were used: 25-35/3-7/1 (TR/TE/excitation), a flip angle of 20°, five slabs, an effective section thickness of 0.8 mm, a field of view of 200^2 mm and a matrix of 256 × 256 pixels. The TOF images were reconstructed using maximum intensity projection and volume-rendering algorithms.

2.3. Image quality analysis

According to a previously used classification [21], two observers classified the image quality of each dataset into four categories: poor, not adequate for diagnostic purposes (0); fair, suboptimal for diagnostic purposes (1); good but slightly lower quality compared to excellent, still useful for diagnostic purposes (2); excellent, high quality for diagnostic purposes (3).

2.4. MRI WMH volume and number analysis

The volume of the WMH was quantified using a semi-automated segmentation technique (Jim, Xinapse System, Leicester, UK). An experienced neuroradiologist [**blinded for peer review**] performed the analysis considering as WMH every hyperintense white matter areas on FLAIR images that were not related to small vessel infarcts, that where excluded manually by the neuroradiologist. The software automatically calculated the volume adding the areas identified by the operator. For each hemisphere the WMH was classified according to the vascular territories (ACA, MCA and PCA) and according to the involvement of the periventricular (PVWM) or deep white matter (DWM).

2.5. CoW analysis

Within the CoW, we searched for the following seven arteries: the anterior communicating artery (AcoA), the two A1 segments of the ACA, the two P1 segments of the PCA, and the left and right posterior communicating arteries (PcoA). According to *Hoksbergen* et al. [22] we used a forced-choice method to classify the presence or absence of the vessel and those arteries that could not be visualised were defined as absent, whereas when visualised were defined as present. The analysis was performed by two neuroradiologists, blinded to clinical data, with 9 and 7 years of experience; they reviewed the TOF source data and the maximum intensity projection images independently. In the case of disagreement, a consensus was reached by consulting a third senior neuroradiologist with 11 years of experience in MRA imaging (Fig. 1).

2.6. Statistical analysis

The normality of each continuous variable group was tested using the Kolmogorov-Smirnov *Z* test. Continuous data were described as the mean value ± SD whereas non-gaussian with median. The inter-observer concordance and the comparison between the PVWMH and DWMH were tested using the Wilcoxon test.

Mann-Whitney test was applied to verify the presence of a statistically significant difference of the volume of WMH in the vascular territories (ACA, MCA and PCA) between normal CoW configuration and each type of variant. The same procedure was