White Matter Changes on Magnetic Resonance Imaging: A Risk Factor for Stroke in an African Population?

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Background: White matter changes are frequently observed incidental findings in elderly individuals. Many studies in Europe and the United States have assessed the association of white matter changes with stroke and other diseases. No similar study has been conducted in sub-Saharan Africa, where risk factors for stroke differ. Our objective was to explore the association between severity of white matter changes (based on visual rating scales) and stroke in a Nigerian population. *Methods:* Magnetic resonance imaging (MRI) scans of 50 patients were retrospectively assessed and scored using 3 different visual rating scales (by Fazekas et al, Scheltens et al, and Manolio et al). The scores were classified as either mild or severe. Clinical indications and MRI scan results were classified into vascular (stroke) and nonvascular groups. The association between severity of white matter changes and stroke on MRI was explored using the Student *t* test, the Chi-square test, and multiple regression analysis at an alpha level of .05. *Results:* White matter changes were consistently and significantly more severe in patients with stroke than in patients without stroke ($.01 \leq P < .001$; odds ratios 4.58 and 13.3, respectively) using the 3 visual rating scales. This finding was independent of age and gender as confirmed by regression analysis (adjusted odds ratios 4.8 and 9.2; $.015 \leq P \leq .003$). *Conclusions:* Our findings suggest that severity of white matter changes in Nigerians may be a significant risk factor for stroke independent of age and gender. Prospective larger studies will be required to confirm its role in predicting stroke and stroke recurrence independent of other vascular risk factors, such as hypertension, diabetes, and cardiac diseases. **Key Words:** Africa—magnetic resonance imaging—risk factors—stroke—white matter changes—white matter hyperintensity.

Magnetic resonance imaging (MRI) scans of the brains of elderly individuals frequently reveal white matter changes (WMCs), particularly in patients with vascular risk factors, cerebrovascular diseases, and cognitive and motor impairment.[1-4]

The clinical significance of WMCs, especially in otherwise normal individuals, is still incompletely understood, and its pathogenesis is also still under investigation.[5-7] The widely accepted opinion at the moment is that WMCs represent the radiologic appearance of a vascular process linked mainly with cerebral small vessel changes,[8,9] resulting in chronic or transient but repeated hypoperfusion of the white matter. The hypoperfusion results in an incomplete form of infarction with disruption of the blood–brain barrier, leading to chronic leakage of plasma into the white matter and activation of astrocytes.[8] Activated and swollen astrocytes, typically seen in areas of WMCs, may contribute to the alterations commonly detected by MRI.

Different visual rating scales have been used in the assessment of WMCs. Existing rating scales are heterogeneous with regard to exact morphologic description, including anatomic distribution of the lesions—whether periventricular or deep WMCs—and diameter of the lesions. Differences in the visual rating scales used may explain some of the inconsistencies in previous studies.[10]

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There has been increasing evidence regarding the prevalence, clinical significance, and prognostic value of WMCs. Minimal changes are known to be invariably common in the general population, and there are sufficient data to suggest that the mildest degree of white matter hyperintensities (WMHs) can be considered an almost normal finding in the brains of elderly patients.[3,11] However, there is also an increasing indication that moderate to severe WMHs are associated with cerebrovascular disease, migraine, motor and gait disturbances, depressive symptoms, urinary disturbances, and some cognitive deficits.[12,13] The presence of WMH has been identified as a marker of less favorable prognosis in acute stroke settings, and like other biologic markers of underlying disease, there is a need to carefully study, assess, and quantify WMHs to understand the depth of its relevance in stroke.

Several previous studies conducted to evaluate cerebral white matter on MRI have been in developed countries, primarily in Europe and North America. These studies, which assessed the association between WMCs and aging as well as other vascular risk factors and clinical correlates, have reported variable results.[5,10,14,15] These inconsistent results cannot be extrapolated to African countries and other developing countries where the profiles and patterns of risk factors for stroke are different.[16,17] An Internet literature search did not reveal any similar study in the sub-Saharan West African population, probably because of the limited availability of advanced neuroimaging facilities in this region.

Our objective was to use multiple universally accepted visual rating scales to quantify the severity of WMCs on MRI and explore its possible association with stroke in a sample of Nigerian patients ≥45 years of age with varying clinical indications for MRI.

Methods

Over a 6-year period (2006-2011), 395 MRI scans of the brain were performed for various reasons at the University College Hospital, Ibadan, in Ibadan, Nigeria. The images were acquired using a low field, 0.2-Tesla, MRI machine (Magnetom Concerto; Siemens, Erlangen, Germany). We retrospectively reviewed these cases and selected all patients ≥45 years of age with WMHs and found only 50 patients eligible. The images were evaluated by 2 independent raters (G.I.O. and B.P.Y.) with differing levels of experience, and a consensus was reached. T1- and T2-weighted axial images were available for all 50 patients. These were complemented by fluid-attenuated inversion recovery (FLAIR) MRI sequences to allow for better separation and identification of WMHs and cerebrospinal fluid.

We used 3 widely available visual rating scales for our assessment: the Manolio scale,[18] the Fazekas scale,[14] and a modified Scheltens scale.[5,19] A modified Scheltens scale was used that, unlike the original, did not include scoring of lesions in the basal ganglia and infratentorial region (see Appendix). This allowed for uniformity among the 3 rating scales used, because the basal ganglia and infratentorial region were not included in the others. For scales scoring periventricular and deep WMCs separately (Fazekas et al and Scheltens et al), we summed the 2 subscores to obtain a total score, which was compared with the one obtained on the Manolio scale.

The severity of the WMH was stratified into "mild" or "severe" (Fig 1) for each of the visual rating scales by dividing the total scores by 2. The values below the median were regarded as mild; scores above the median were considered severe.

The clinical indication for MRI, as documented in the referral notes for imaging by the managing physician, was stratified into "vascular" and "nonvascular" groups. The vascular group had a clinical history that was mainly suggestive of stroke, while the nonvascular group had a clinical history suggestive of tumor, infection, or nonspecific symptoms and signs. MRI findings were also stratified in a similar fashion, with vascular MRI findings including both hemorrhagic and ischemic strokes.

The association between a patient's sex and WMH severity score was tested using the Student t test. A correlation between a patient's age and WMH severity score was assessed with the Spearman rank analysis. The relationship between WMH severity score and clinical indication (non-WMH vascular vs. nonvascular) for the MRI scan was analyzed using the Student t and Chi-squared tests. Similarly, the association between WMH severity and MRI findings of stroke was also assessed with the Student t and Chi-squared tests. The scores were ordinal and all had a normal distribution. We used the Levene's test for normality to select the appropriate t and P values.

Statistical analyses were performed with SPSS software for Windows (version 16.0; SPSS Inc., Chicago, IL), and $P < .05$ was considered statistically significant.

Results

All patients evaluated were Nigerians of African descent. The study groups consisted of 28 (56%) men and 22 (44%) women between 45 and 95 years of age (mean 63 years [SD 10.49]). Twenty-seven (54%) had vascular clinical indications for MRI; 21 (42%) patients had a MRI finding of stroke (96% ischemic; 4% hemorrhagic). The mean WMH severity scores for patients with vascular clinical indication for MRI and MRI findings of stroke were consistently higher for all the visual rating scales (Tables 1 and 2). There was strong correlation between the visual rating scales ($P < .001$; $\rho = 0.78$-0.83).

In all visual rating scales, patients who had vascular clinical indication and vascular MRI findings had significantly more severe WMHs compared with those with nonvascular indications and nonvascular MRI