

The Prevalence of Magnetic Resonance Imaging Hyperintensity in Migraine Patients and Its Association with Migraine Headache Characteristics and Cardiovascular Risk Factors

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ABSTRACT

Objectives: To determine the frequency of hyperintense foci in migraine patients and the relationship with migraine headache characteristics and cardiovascular risk factors. **Methods:** Ninety patients with migraine headache (70 without aura and 20 with aura) were enrolled and interviewed. Information on their headache (severity, frequency, and mean disease duration) and other related data was obtained by completing a clinical checklist. Subsequently, brain magnetic resonance imaging (MRI) was performed and each patient was then evaluated for hyperintense lesions. **Results:** Of the 90 patients, 29 (32%) had silent hyperintense lesions on their MRI. The mean age of the patients with hyperintense foci was 41 years while those with no lesions was 33 years ($p < 0.010$). Supratentorial hyperintense lesions represented the majority of lesions in the patients ($n = 46$, 63%). Moreover, 56.3% of the lesions ($n = 41$) were located within the right hemisphere. Cardiovascular risk factors such as smoking, serum cholesterol, oral contraceptive pills use, and body mass index (BMI) were not significantly different in these two groups ($p > 0.050$). The lesions were found significantly more frequently in the patients who experienced chronic migraine ($p = 0.032$). **Conclusion:** Our study adds weight to the theory that disease duration has a key role in the formation of hyperintense brain lesions. Certain cardiovascular risk factors such as sex, smoking, serum cholesterol, and BMI, do not affect the presence or absence of such lesions, suggesting that the relationship between migraine and these lesions may be directly due to the effects of migraine itself.

Migraine is a chronic and recurrent vascular headache, and is one of the most common diseases in the general population.¹ It is a complex brain disorder and its pathogenesis and mechanism has been widely investigated. Although migraine has been associated with various comorbidities,¹⁻³ structural brain lesions also seem to be linked to the disease and are believed to be of vascular origins.⁴⁻⁶ Evidence suggests that migraine is associated with an increased risk of silent infarct lesions and high signal intensities observed at the time of performing magnetic resonance imaging (MRI).⁷⁻¹² It has been reported that female patients with migraine with a longer duration of the disease and a higher frequency of attacks are more likely to develop lesions.¹²⁻¹⁴

Silent infarct lesions, also known as white matter hyperintensities (WMH), are referred to as obvious lesions with MRI infarction features and are not accompanied by clinical symptoms or other stroke-related signs.¹⁵ Although their pathogenesis is probably multifactorial, the clinical importance of these lesions is yet to be understood. These hyperintense lesions are commonly considered to be ischemic, which is logical given their association with vascular risk factors.^{16,17} While seemingly transient ischemic events in posterior blood circulation of the brain are responsible for such lesions,¹⁸⁻²⁰ other factors have also been put forth regarding the pathophysiology of these abnormalities. These include glutamatergic excitotoxicity,²¹ hyperlipidemia, hypertension,

smoking,²² immunogenic demyelination of white matter,²³ mitochondrial dysfunction,²⁴ endothelial dysfunction,^{25,26} attack-related oligemia and focal hypoperfusion,²⁷ and vasoactive drugs like triptans or ergots.²⁸

Several studies have investigated the risk factors associated with brain lesions in the MRI of migraine headache patients, although a consensus is yet to be reached on this matter. The aim of this study was to evaluate the frequency of infarct lesions in the MRI of migraine patients, and identify the relationship between migraine characteristics and other clinical risk factors.

METHODS

We conducted a prospective cross-sectional study between January 2009 and December 2010. We included participants with a history of headache, who met the 2004 migraine criteria as defined by the Headache Classification Committee of the International Headache Society (IHS).²⁹ Patients with major comorbidities and history of organic diseases, such as hypertension and cardiac disease, were excluded from the study along with those with diabetes mellitus, endocrine dysfunction, oncological and hematological diseases, infectious diseases, demyelinating disorders of the central nervous system, genetically inherited disorders, and patients with a history of head trauma and diseases associated with brain hyperintensities without migraine. A total of 90 patients with migraine headache were enrolled (69 women and 21 men) aged between 10 and 82 years old (mean 36.09 ± 13.17 years). Seventy patients had migraine without aura (77.8%) and 20 patients had migraine with aura (22.2%).

In a face-to-face interview in our neurological diseases clinic, standardized questionnaires were employed to ascertain information concerning patients' demographics, medical history, oral contraceptive pills (OCP) use, and other habits such as smoking. Chronic migraine was defined as more than 15 days of headache per month with each headache lasting for at least four hours over a period of three months or more in people with prior migraine diagnosis.²⁹ Episodic migraine was defined as less than 15 days of headache per month.²⁹

Institutional ethics committee approval was obtained for this study and written informed consent was obtained from all participants.

A group of trained staff measured the height and weight of the patients and took blood samples to determine total cholesterol levels. During the interview, participants were asked standardized questions regarding their headache, including information on mean disease duration, frequency of episodes, the intensity of pain, characteristics, location of the pain, aura, and associated features such as nausea and sensitivity to light and sound. The visual analogue scale (VAS) score was used to measure the intensity of the headache. Participants then underwent cerebral MRI (Avanto 1.5 T scanner, Erlangen, Germany). T2-weighted axial, coronal, and sagittal planes and FLAIR sequence in axial planes were obtained. The characteristics of the lesions were visualized in each plane. Employing a standardized assessment grade, a neuroradiologist, unaware of the participants' headache status and other clinical data, reviewed the brain scans. Based on the brain MRI findings, patients were divided into two groups: patients with hyperintensities and patients without hyperintensities.

Data was analyzed using SPSS version 18 (SPSS Inc., Chicago, USA). Student *t*-test was used for continuous variables and Chi-Square test for categorical variables. A *p*-value of less than 0.050 was considered statistically significant.

RESULTS

Of the 90 patients enrolled in this study, 29 patients (32.2%) had silent hyperintense lesions in their MRI. Amongst the 73 lesions detected in this population, left supratentorial white matter was the most common site of hyperintense foci (25 lesions, 34.2%), followed by right supratentorial white matter ($n=21$, 28.7%) and right pons ($n=7$, 9.5%). In total, left and right supratentorial hyperintense lesions represented the majority of all hyperintense lesions ($n=46$ lesions, 63.0%) in the whole brain while 37.0% of the lesions ($n=27$) were found in infratentorial white matter. Moreover, 56.2% of the lesions ($n=41$) were located within the right hemisphere of the brain.

Patients with hyperintense foci were significantly older than those without (mean =41.2 years vs. 33.6 years; $p<0.050$). No significant relationship was found between the number of hyperintense lesions detected by MRI and gender, history of smoking, body mass index (BMI), cholesterol level, and OCP use [Table 1]. MRI hyperintense foci were

Table 1: The relationship between MRI hyperintense lesions and cardiovascular risk factors.

Risk factor	Patients with hyperintense lesion	Patients without hyperintense lesion	p-value
Male (%)	13.8	27.8	0.111
Female (%)	86.2	72.2	0.111
Age (years)	41.2	33.6	0.010
Smoking (%)	6.6	10.3	0.136
Mean BMI (kg/m ²)	26.4	24.8	0.136
Serum cholesterol (mg/dL)	208	189	0.264
Duration of OCP use (years)	1.69	0.5	0.215

OCP: oral contraceptive pills; BMI: body mass index

significantly associated with the duration of migraine disease (mean =16 years vs. 10.4 years; $p < 0.050$). According to the MRI findings, hyperintense lesions were more frequent in patients who experienced chronic migraine compared with patients with episodic migraine ($p < 0.050$). No meaningful relationship was detected between overall headache frequency and headache intensity, the presence of aura, sumatriptan dosage, duration of prophylactic medications, and headache location [Table 2].

DISCUSSION

The association between migraine and intracranial lesions has been discussed by many authors.^{5-8,18-20,28,30} However, the underlying mechanism by which migraine causes brain structural lesions is still under debate.⁷ Swartz and Kern,³¹ in a meta-analysis, reported a four-fold increased risk of white matter lesions in patients with migraine. Based on a large population-based sample study, migraine was highly associated with an increased risk for deep white matter lesions in women,²⁸ which was in accordance with our findings since the majority of the patients

with hyperintensities were women. However, the authors were not able to correlate the presence or absence of aura with the risk for subclinical lesions.

Although the literature significantly lacks a comparable control group,⁴ it has been proven that migraine with aura has the highest risk for subclinical infarction in the cerebellum probably due to hypoperfusion in the posterior circulation of the brain.^{12,28} In a study by Kruit et al,¹² it was reported that these lesions were more prevalent in patients with aura migraines than those with regular migraines. On the contrary, Cavestro et al,³² reported that 33% of regular migraine patients and 24% of aura migraine patients presented with some kind of brain lesion. The source of this discrepancy is still unclear; however, ischemic events including stroke have been related to migraine.^{2,10,33}

Our results further extend the findings by Kurth et al,⁸ where most lesions were located outside the cerebellum and brain stem. In contrast, Kruit et al, indicated that patients suffering from aura migraine were more likely to have lesions in posterior brain circulation (cerebellum and brain stem).^{18,20,28} In our study, the supratentorial regions were the sites

Table 2: The connection between MRI hyperintense lesions and clinical characteristics of migraine.

Migraine characteristic	Patients with hyperintense lesion	Patients without hyperintense lesion	p-value
Disease duration (years)	16	10.4	0.008
Intensity of the pain	7.3	7.5	0.613
Duration of prophylactic medications (years)	1.6	1.7	0.953
Sumatriptan dosage (tablets/month)	0.6	1.5	0.341
Aura (%)	17	25	0.310
Frequency (numbers/month)	14	11	0.923
Chronic migraine* (%)	24	8	0.032

*Chronic migraine is a migraine headache occurring for at least 15 days per month over a period of at least three months.

where hyperintense lesions were most prevalent, a finding similar to Cavestro et al,³² who found that the subcortical supratentorial region was the most common site of brain lesions. Infratentorial lacunar lesions were present in about 2% of MRI scans.

Despite the strong relationship proposed^{6,30} between aura migraines and more intensified or deeply located lesions in white matter, the mechanism has not been well documented. Immediate hypoperfusion after a migraine attack has been suggested as an underlying mechanism.³⁴⁻³⁶ However, some researchers have observed delayed hyperemia following hypoperfusion during migraine episodes.³⁶

Supporting evidence convincingly points to the relationship between migraine and cardiovascular risk factors such as dyslipidemia, smoking, hypertension, and BMI.^{2,4-6,22} The frequency of lesions in one study³⁷ was 34.6% in smokers and 29.8% in non-smokers, which is higher than our findings. Similarly to our study, other researchers did not find higher risks of hyperintense lesions in patients with high cholesterol.³⁷⁻³⁹ Scher et al,²² reported that patients with aura migraine run a higher risk of cardiovascular disease compared to individuals without migraine.

Some studies have shown that hyperintense lesions are not affected by any history of hypertension, diabetes, smoking, hypercholesterolemia, and OCP use.^{31,40} Similarly, our study did not reveal any association between hyperintense lesions and smoking, hypercholesterolemia, and OCP use. Some findings are in contrast or in line with our results, which could be due to the smaller sample size of our study compared to meta-analyses and other large population-based studies.

According to the MRI, there was a significant association between hyperintense lesions and age, severity of migraine, and headache duration. Similar to our research, female patients and patients with a higher frequency of migraine attacks and longer duration of the disease are reported to have a higher risk of developing hyperintense lesions.^{12,13} Kurth et al,⁸ reported similar findings indicating that any history of severe headache would be related to increased hyperintensities in white matter. Unlike our research, their study enrolled older patients and was unable to draw any relationship between age and hyperintense lesions. It is suggested that the type of migraine, attack duration, and comorbid

conditions can also influence the risk of developing such lesions.^{12,13}

Generally, the absence of a control group for comparison is considered a pitfall in the literature. Unfortunately, due to ethical issues, we were unable to benefit from a control group and only had a small sample size, which was another limitation of our study. Future studies would seek to determine the effects of different migraine treatment options on the prevalence of hyperintense foci in MRI through conducting a randomized clinical trial.

CONCLUSION

Our study adds weight to the theory that disease duration, alongside various other factors, has a key role in the formation of hyperintense brain lesions. Cardiovascular risk factors, such as gender, smoking, serum cholesterol, and BMI, do not cause such lesions suggesting that the relationship between migraine and these lesions may be independent of the ischemic cardiovascular risk factors and may be directly related to the effects of migraine. A better understanding of the pathophysiology of migraine, and hyperintense lesions, migraine prophylaxis and effective treatments may reduce the risk of developing lesions.

Disclosure

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