

# Archives of SID Leukoaraiosis in the North American and Persian stroke patients

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## Abstract

**Intraduction:** Leukoaraiosis (LA) or white matter thinning and rarefaction is common in the patients with stroke.

**Materials and Methods:** This prospective clinical study was conducted on 100 consecutive patients in Mackenzie hospital, Canada and 100 consecutive stroke patients in Valie Asr hospital, Iran during 2004. Diagnosis of ischemic stroke and LA was performed by stroke neurologists using CT scan. The effects of race, gender, age groups, hypertension, diabetes, hypercholesterolemia and smoking on the frequency rate of LA were evaluated. Chi-Square, Fisher and Regression tests served for statistical analysis and  $p < 0.05$  was declared as significant.

**Results:** In the whole studied patients, 12 males and 30 females had LA which was significantly more frequent in females ( $p = 0.002$ ). The frequency rate of LA was the same in the North American and Persian stroke patients ( $p = 0.99$ ). Stroke patients aged  $\geq 65$  years were significantly more preponderant for LA than patients  $< 65$  years ( $p = 0.049$ ). LA was significantly more frequent in the hypertensive patients ( $p = 0.04$ ). The effects of diabetes, hypercholesterolemia and smoking on the frequency rate of LA were not significant.

**Discussion:** Age, female gender and hypertension are the risk factors of LA. There is no difference in the frequency rate of LA between the North American and Persian stroke patients.

**Keywords:** Leukoaraiosis, Risk Factors

## Introduction

Leukoaraiosis (LA) means thinning or rarefaction of the cerebral white matter. LA is associated with minor cognitive impairment in otherwise normal individuals as well as stroke patients and in the advanced grades can lead to vascular dementia<sup>(1)</sup>.

LA is seen in the clinical cases of dementia, non-demented cerebrovascular patients, healthy elderly subjects and various dysmyelinating conditions. LA is classified as a variant of atherosclerosis that selectively involves the penetrating arterioles of the periventricular areas, resulting in chronic ischemia and progressive cognitive decline<sup>(1)</sup>. LA represents deeply placed watershed infarcts. The combination of atherosclerosis and the reduced perfusion pressure results in multiple lacunar infarctions, ischemic demyelination,

edema, ependymal disruption and gliosis<sup>(2)</sup>. LA has prognostic implications because its presence increases the risk of stroke not only in the patients with transient ischemic attacks and minor stroke but also in general population<sup>(3)</sup>. In addition, LA increases the risk of intracerebral hemorrhage in the patients receiving anticoagulation for secondary prevention of cardioembolic strokes<sup>(3)</sup>. LA is more prevalent in the patients with the history of stroke rather than matched controls<sup>(2)</sup>. In neuroimaging, the incidence and severity of LA is related to the age and some vascular risk factors. The fact that in spite of intensive control of the vascular risk factors in the last decades, the incidence of LA and vascular dementia has not changed significantly<sup>(2)</sup>, reveals the need for further research.

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### Materials and Methods

100 consecutive ischemic stroke patients admitted in Mackenzie hospital, Canada and 100 consecutive ischemic stroke patients admitted in Valie Asr hospital, Iran during 2004 enrolled in a cross-sectional and prospective study. Diagnosis of the ischemic stroke was made by the stroke neurologists based on WHO criteria<sup>(4)</sup>. LA was defined on baseline CT scan as the symmetrical hypodensity in the periventricular and subcortical white matter. These are poorly marginated, patchy or punctuate and non-dysplacating lucencies. LA is more concentrated around frontal horns as well as the trigones of the lateral ventricles in mirror-image locations<sup>(5)</sup>. Patients were included in <65 and ≥65 years age groups. Hypertension was defined as using antihypertensive medication or patients with two blood pressure values (at least 1 week apart) of >140/90 mm/Hg. Administration of antidiabetic medication or a fasting blood glucose >6.4 mmol/L or >126 mg/dL were the definitions of diabetes mellitus. Hypercholesterolemia assumed as using lipid lowering medication or fasting cholestrole > 5.2 mmol/L or >200 mg/dL. Patients who smoked more than 5 cigaretts per day in the recent year were defined as smoker. The effects of race, gender, age group and the vascular risk factors on the frequency rate of LA were analysed by Chi-Square, Fisher exact and multiple logistic regression tests and  $p < 0.05$  was declared as significant. In neuroimaging, cerebral infarctions were classified as small vessel and large vessel territory infarcts. Small vessel territory or lacunar infarcts defined as subcortical infarcts with a diameter of <2cm and large vessel territory infarcts consisted of the cortical infarcts or subcortical infarcts with a diameter >2cm<sup>(6)</sup>.

### Results

200 ischemic stroke patients (98 females, 102 males) with mean age of  $71.88 \pm$

10.99 were evaluated. 21% of the North American and Persian stroke patients had

LA without difference in race, OR=1, CI (0.51-1.98), ( $p=0.99$ ). In the age groups <65 and ≥65 years, the LA frequency rate had no significant difference between the North American and Persian stroke patients, ( $df=1$ ,  $p=0.072$ ), ( $df=1$ ,  $p=0.588$ ) respectively. LA was present in 29.4% of the females and 12.2% of the males with stroke, showing a significant female preponderance, OR=3.295, CI (1.54-7.05), ( $p=0.002$ ).

Stroke patients aged ≥65 years were significantly more preponderant for LA than patients <65 years, OR=2.54, CI (1-6.43), ( $p=0.049$ ). The frequency rate of LA was significantly higher in hypertensive than non-hypertensive patients, OR=1.36, CI (0.67-2.75), ( $p=0.04$ ). LA frequency rate was not significantly different between diabetic and non-diabetic patients, OR=0.92, CI (0.41-2.04), ( $p=0.841$ ).

The difference of LA frequency in the hypercholesterolemic and smoker patients were not significantly higher than the patients without these risk factors, [OR=0.86, CI (0.40-1.86), ( $p=0.71$ )] and [OR=0.618, CI (0.20-1.89), ( $p=0.40$ )] respectively.

LA was more frequent in the patients with small vessel than large vessel territory infarcts without significant preponderance, OR=0.603, CI (0.28-1.26), ( $p=0.181$ ).

### Discussion

This clinical study was conducted by using CT scan technology. Although MRI have more sensitivity than CT (100% versus 72%) for detection of LA, however its specificity is lower than CT (88% versus 100%)<sup>(1,6)</sup>. The frequency rate of LA was the same in the North American and Persian stroke patients which are two different white races. A US study on the white and black americans has shown similar results<sup>(7)</sup>. However in another US

study white race was more preponderant for the ventricular enlargement and sulcal

widening than blacks<sup>(8)</sup>. Females had 3.29 times more risk than males for the development of LA in our study groups which is congruent with the Rotterdam

scan study. This may underlie the finding of a higher incidence of dementia in women than in men, particularly at the later age<sup>(9)</sup>. Gender preponderance for LA was not found in the US and Turkish studies<sup>(7,10)</sup>. However a similar study conducted in Bethesda showed male gender preponderance of LA<sup>(8)</sup>. The frequency of LA in our study groups lies in the range of 4.3%-38% of other studies worldwide<sup>(2)</sup>. This wide range of prevalence is due to the differences in neuroimaging technology and LA definitions. This centered pilot study was conducted in the patients with the ischemic stroke and could not show the frequency rate of LA in the North American and Persian general population. In our study groups, the stroke patients aged  $\geq 65$  years had 2.54 times more risk than the patients  $< 65$  years for the development of LA by adjusting gender effect. Hachinski et al found LA in 11% of the stroke patients in the fourth decade and 65% of those in the seventh decade<sup>(11)</sup>. In fact, aging and hypertension are the important risk factors of LA in our stroke patients. LA was strongly

associated with the age and hypertension in the other case-control and cohort

studies<sup>(7,8,10,12)</sup>. Only about one fourth of the elderly patients with hypertension develop LA, this suggests that factors other than age and vascular risk factors must be involved in the development of LA, genetic factors being one<sup>(3)</sup>. Although some studies has shown significant effect of other vascular risk factors such as diabetes, hypercholesterolemia and smoking<sup>(12,13,14)</sup>. However the results of our study and some other US studies does not support this idea<sup>(5,15)</sup>. Bogousslavsky et al had confirmed that LA is significantly more frequent in the patients with small artery disease and lacunar infarction<sup>(16)</sup>. Although LA was more frequent in our stroke patients with lacunar infarction, however this difference is not significant. The reason of this discrepancy could be the admission indications in our two centered study and swiss study conducted by Bougousslavsky. Stroke patients with mild deficits were not admitted in our hospitals.

### Conclusions

Our results confirm that development of LA is correlated with aging and hypertension. LA is commonly associated with small artery disease.

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# لکوآریوزیس در مبتلایان به سکنه مغزی آمریکای شمالی و ایرانی

خلاصه

لکوآریوزیس یا تحلیل رفتن و نازک شدن ماده سفید مغز در مبتلایان به سکنه مغزی شایع می باشد .

این مطالعه بالینی آینده نگر بر روی ۱۰۰ بیمار پی در پی سکنه مغزی بستری در بیمارستان مکتزی کانادا و ۱۰۰ بیمار پی در پی سکنه مغزی بستری در بیمارستان ولیعصر ایران در سال ۲۰۰۴ انجام گرفت. تشخیص سکنه مغزی ایسکمیک و لکوآریوزیس توسط متخصص داخلی مغز و اعصاب عروقی و انجام سی تی اسکن مغز بود. تاثیر نژاد، جنسیت، گروه سنی، پرفشاری، دیابت، هیپر کلسترولمی و مصرف سیگار در فراوانی نسبی لکوآریوزیس بررسی شد. آزمون های کای اسکوار، فیشر و رگرسیون برای تحلیل آماری بکار رفته و از (  $p < 0.05$  ) بعنوان معنی دار تلقی شد. در مبتلایان به سکنه مغزی بطور کلی ۱۲مرد و ۳۰ زن مبتلا به لکوآریوزیس بودند که در زنان از فراوانی بیشتری برخوردار بود (  $p < 0.002$  ) فراوانی نسبی لکوآریوزیس در بیماران آمریکای شمالی و ایرانی یکسان بود. لکوآریوزیس در گروه سنی بیشتر یا مساوی ۶۵ سال فراوانی نسبی بیشتری نسبت به گروه سنی کمتر از ۶۵ سال دارد (  $p < 0.05$  ). لکوآریوزیس بطور معنی داری در بیماران با پرفشاری شایعتر بود، پی=  $0.04$  . دیابت، هیپر کلسترولمی و مصرف سیگار تاثیر معنی داری بر فراوانی نسبی لکوآریوزیس نداشتند. کهولت سن، جنس مونث و پرفشاری عوامل خطر ساز لکوآریوزیس هستند و تفاوتی از نظر فراوانی نسبی آن در بیماران آمریکای شمالی و ایرانی وجود ندارد.

واژه های کلیدی: لکوآریوزیس، عوامل خطر ساز.