

## Atherosclerosis Surrogate Marker in Diabetic Patients

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### Abstract

**Objective:** Duplex ultrasonography is a non-invasive, non-expensive screening test for carotid disease. Intima media thickness (IMT) is appropriate for atherosclerosis process diagnosis. Leukoaraisis (LA) increase the risk of cerebrovascular accident (CVA). LA patients need preventive medication for CVA. IMT is a non-invasive diagnostic and prognostic test in LA. The aim of this study was evaluate the carotid IMT and LA in diabetic patients as atherosclerosis surrogate marker.

**Materials and Methods:** The case-control study was done on 100 diabetic patients and 100 controls. They were selected by simple sampling method in Shaheed Sadoughi MRI unit. Two groups member were matched by age and sex. The patient's information (age, sex, weight, height, past medical history, smoking history, ischemic heart disease (IHD), CVA and past medication) according the study checklist was collected. All statistical analysis was done by SPSS21.

**Results** Totally 200 patients were studied, 102 in normal group and 98 in diabetic group. The mean age of patients was 64.39 ( $\pm 9.12$ ) and 47% participants were male. There were no statistical differences between hypertension and hyperlipidemia frequency in two groups ( $P$ -value $>0.05$ ). The mean of left CIMT was 0.856 ( $\pm 0.202$ ) in normal and 0.962 ( $\pm 0.171$ ) in diabetics groups ( $P$ -value: 0.026). The mean of right CIMT was 0.853 ( $\pm 0.215$ ) in normal and 0.973 ( $\pm 0.188$ ) in diabetics groups ( $P$ -value: 0.024). The LA was significantly more prevalent in diabetic patients ( $P$ -value:0.001).

**Conclusion:** LA increases the risk of CVA and dementia. The LA pathology is unknown. The epidemiological studies revealed the age, diabetes, smoking and atherosclerosis are related with LA. Our findings showed that CIMT as an atherosclerosis marker was higher in LA patients than control group.

**Keywords:** Leukoaraisis, Intima media thickness, Duplex ultrasonography, Diabetes.

An increased carotid intima-media thickness was associated with cardiovascular risk factors, cardiovascular disease (CAD), and atherosclerosis in the arterial system (1-7). Leukoaraisis (LA) is known as white matter

changes (8). LA is associated with cognitive impairment (8-9), gait abnormalities, falls, and late-onset depression. LA is identified as hyperintensities in T2 sequences and fluid-attenuated inversion recovery (FLAIR) in magnetic resonance imaging (MRI) or

hypodensity with ill-defined margins in computed tomography (CT) in the areas of cerebral white matter (10-13).

LA is known as independent risk factor of stroke (14-15), poor stroke outcome (16). LA increases the risk of cerebro-vascular accident (CVA) (17-18). LA patients need preventive medication for CVA (19). Diabetes as CVA and CAD risk factor may be associated with LA. Although, increasing evidence indicates a relationship between carotid atherosclerosis and LA, but LA may be partially reversible in patients with carotid artery stenosis (20-23).

Intima media thickness (IMT) is appropriate for atherosclerosis process diagnosis especially in diabetic patients (24). Non-invasive assessment of IMT is widely used as an intermediate diagnostic tool in atherosclerosis process (25-26). There is a growing belief that carotid IMT can be used as an indicator of generalized atherosclerosis. Duplex ultrasonography is a non-invasive, non-expensive screening test for carotid disease. IMT may be useful as a non-invasive diagnostic and prognostic test for atherosclerosis diagnosis in diabetic patients (27-30). The aim of this study was evaluate the carotid IMT and LA in diabetic patients as atherosclerosis surrogate marker.

## Materials and Methods

The case-control study was conducted on 100 diabetic patients and 100 controls. They were selected by simple sampling method in Shaheed Sadoughi MRI unit. Two groups member were matched by age and sex. The patient's information (age, sex, weight, height, past medical history, smoking history, ischemic heart disease(IHD), CVA and past medication) according the study checklist was collected.

To measure carotid intima-media thickness, ultrasonography of the common carotid artery, carotid bifurcation, and internal carotid artery of the left and right carotid arteries was performed with Sonoline G60 Model :Ay 15 CUZ • Simens and Linear Array Transducer 7-10 MHZ. On a longitudinal, two-dimensional

ultrasound image of the carotid artery, the anterior (near) and posterior (far) walls of the carotid artery are displayed as two bright white lines separated by a hypo-echogenic space. The distance between the leading edge of the first bright line of the far wall (lumen-intima interface) and the leading edge of the second bright line (media-adventitia interface) indicates the intima-media thickness. LA was diagnosed by MRI. The imaging method was T2-weighted spin-echo [repetition time/echo time (TR/TE)=5800/96 ms], T1-weighted spin-echo (TR/TE=520/14 ms), and FLAIR (TR/TE=8500/96 ms; inversion time=2100 ms) images. LA was described as a focal lesion  $\geq 2$  mm in diameter, with hyper-intensity on T2-weighted and FLAIR images and without prominent hypo-intensity on T1-weighted images. The thickness of MRI slices was 4 mm, and 3 sections of the axial, sagittal, and coronal 2D views were used for LA diagnosis.

All statistical analysis was done by SPSS21.

## Results

Totally 200 patients were enrolled (98 in diabetic and 102 in normal group). The mean age of participants was  $63.39 \pm 9.12$  years old. In diabetic group 51% were male and 49% were female and in control group there were 43% and 57%.

Table 1 describes general characteristics in two groups. Two groups IMT mean was compared. (table2). Additional analysis showed the risk ratio (RR) in right IMT $>1$ , 7.12 with 95% confidence interval (2.48-17.99) and in left IMT $>1$ , 8.82 (2.29-18.86).

## Discussion

The findings in our study indicate that an increased common carotid intima-media thickness is associated with diabetes. Also the LA is more prevalent in diabetic patients. It is important to realize that there were no matching in atherosclerosis risk factors except age and sex.

**Table 1. General characteristics in two groups**

Variables	Diabetes Frequency (%)	Normal Frequency (%)	P-value
Hyperlipidemia	33(33.7%)	27(26.5%)	0.266
Hypertension	36(36.7%)	27(26.5%)	0.118
Carotid Plaque	38(38.8%)	20(19.6%)	0.003
Ischemic Heart Disease	37(37.8%)	22(21.6%)	0.012
La	52(53%)	28(27.5%)	0.001
Smoking	33(33.7%)	15(14.7%)	0.003

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In Turk and et.al study findings was according with our findings (23). But in Saba study which was done in Italy there were significant differences between two groups (24). It should be noticed that there were no matching of atherosclerosis risk factors in two groups.

LA as an important public health problem increases the risk of stroke and dementia (25-27). The pathophysiology of LA is unknown, but LA is correlated with age, hypertension, arteriosclerosis, smoking, and diabetes in epidemiological studies (28-32). Also there is increasing evidence of relationship between large artery atherosclerosis and LA (32).

Our findings showed IMT is increased in diabetic group which was discovered by duplex sonography. The noninvasive assessment of common carotid intima-media

thickness appears to provide a capable method to study the atherosclerosis risk factor in large populations (15-18).

As our study limitations, there were no group matching except age and sex for atherosclerosis. So in future studies, it should be considered.

## Conclusions

The LA frequency was higher in diabetic patients. LA increases the risk of CVA and dementia. The epidemiological studies revealed the age, diabetes, smoking and atherosclerosis are related with LA. Our findings showed that CIMT as an atherosclerosis marker was higher in diabetic patients than control group.

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