

# Carotid doppler ultrasound evaluation in patients with lichen planus

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## INTRODUCTION

Lichen planus (LP) is a chronic and T cell mediated inflammatory mucocutaneous disease, which is not known yet in term of etiology and pathogenesis.

**Background:** Lichen planus is a chronic inflammatory disease associated with an increased risk of subclinical atherosclerosis and cardiovascular diseases. This study aimed to evaluate patients with lichen planus using carotid Doppler ultrasound parameters.

**Methods:** Forty patients with lichen planus and 40 controls were included in this study. Common carotid artery intima-media thickness (CIMT) and the number of atherosclerotic plaque were measured and compared to the control group. Total cholesterol, triglyceride, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) levels were measured. Leptin level (Pg/ml) was measured using the enzyme-linked immunosorbent assay (ELISA) method (Leptin ELISA kit, Orgenium, Finland).

**Results:** Significant difference was found between the groups in terms of CIMT ( $P=0.005$ ). The median range for blood leptin level, triglyceride, cholesterol, and LDL was higher for lichen planus patients than for controls. We found a significant difference between the severity of LP and CIMT ( $P=0.035$ ). No statistical difference was found between LP and the number of atherosclerotic plaque.

**Conclusions:** Our study suggested that measurement of the mean intima media wall thickness of the common carotid artery could be beneficial as a valuable method for early diagnosis of atherosclerosis in lichen planus.

**Keywords:** lichen planus, common carotid artery, doppler ultrasound

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Owing to chronic inflammatory condition, it can enhance the formation of atherosclerotic plaques, and causes disturbances in lipid metabolism <sup>1</sup>.

Several cytokines are involved in lichen planus pathogenesis, and some major independent risk

factors— for cardiovascular diseases in Lp— could suggest it as a component of the metabolic syndrome<sup>2</sup>. In addition, the current literature considers endothelial dysfunction and carotid intima-media thickness (CIMT) important markers of subclinical atherosclerosis and cardiovascular diseases<sup>3</sup>.

Few studies have shown evidence of subclinical atherosclerosis in LP patients than in controls as indicated by increased CIMT, and there are conflicting findings regarding the relationship between LP, its severity or duration and subclinical atherosclerosis risk.

The main objective of this study was to evaluate patients with lichen planus regarding carotid Doppler ultrasound parameters.

## **PARTICIPANTS AND METHODS**

### **Participants and study design**

A total of 40 patients with lichen planus, presented to a dermatology clinic, were included in this study— based on inclusion criteria. Additionally, 40 age, gender matched healthy controls were selected amongst hospital staff, without any known dermatologic and nondermatologic disease. Inclusion criteria for the study group were presence of lichen planus affecting the skin or mucosa that was confirmed according to clinical and biopsy findings. Informed consent was obtained from all included patients before participation as one of the inclusion criteria.

Patients with renal and hepatic, neurologic disorders, lichenoid drug eruption, a history of cardiovascular, cerebrovascular diseases or collagen vascular diseases, smoking habit, thyroid dysfunction, hypertension, diabetes mellitus, pregnancy, malignancy, receiving any systemic lichen planus treatment, steroid, immune-suppressive treatment, lipid-lowering therapy, antihypertensive or hormonal, and anticoagulant drugs were excluded from the study. The participants were recruited from Rohani Hospital of University of Medical Sciences, Babol, Iran, from 2017 to 2018. Demographics and clinical characteristics of patients with lichen planus and healthy controls were assessed.

After 12-hour fasting, 5 cc of blood was taken from each participant. Serum samples were

prepared after coagulation and centrifugation of the whole blood at 1500 ×g for 10 minutes. They were frozen and preserved at –80 °C. Biochemical parameters such as serum cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides (TG) were measured using the photothermic auto analyzer method. Serum leptin level was assessed using the ELISA Kit for the quantitative determination of leptin in the human serum (Leptin ELISA, ME E-0300).

Ultrasound measurement of the mean intima-media wall thickness of common carotid artery was assessed by an ultrasound specialist blinded to the patients' data. All participants were examined in a supine position— neck extended and the head was slightly tilted toward the opposite of the examined side.

A magnified image was recorded from the angle, showing the greatest distance between the interface of lumen–intima and media–adventitia. From this offline image, at least three measurements of the common carotid artery wall were taken approximately 10 mm proximal to the bifurcation (the arterial segment 1 cm proximal to the carotid bulb) to derive the mean intima-media wall thickness of common carotid artery. Ultrasound scanning was performed using carotid duplex high-resolution B-mode equipment (Ultrasound, Diagnostic, Samsung Medison, Sonoace X8, Gyeonggi-do, South Korea) with a 12-MHz linear-array transducer (axial resolution of at least 0.3 mm). The final intima-media wall thickness value represents an average of the intima-media wall thickness resulting from three different points on the right side. Atherosclerotic plaque was diagnosed with a carotid artery wall thickness exceeding 1.5 mm. Both left and right common carotid artery (CCA)s were depicted. The reproducibility of intima-media wall thickness and plaque detection has been well documented.

### **Statistical methods**

Chi-square test and Fisher's exact test, wherever appropriate, were performed for data analysis. Mann–Whitney U-test was used for comparison between serum triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and leptin level. Furthermore, Spearman's correlation test

was used to assess the association between mean intima-media wall thickness and other continuous variables. Statistical analyses were conducted using the SPSS Statistics software. P values < 0.05 were considered statistically significant.

### Ethical considerations

The written informed consent was obtained from all participants.

## RESULTS

Forty patients and 40 healthy controls were included in this review. Table 1 presents the patients' demographical, clinical and biochemical parameters. The patients in the two groups were well balanced in terms of age and body mass index. Although the average level of TG, cholesterol, LDL and leptin was higher in LP patients than in controls, it was not significant. The average level of HDL was lower in the LP group. There was a significant difference between the groups in terms of CIMT ( $0.68 \pm 0.14$  mm vs.  $0.59 \pm 0.12$  mm,  $p=0.007$ ).

The average right and left CIMT was significantly higher in LP patients than in controls. The number of atherosclerotic plaques in CCAs was higher in the patients. There was a correlation between CIMT and age. No correlation was found between CIMT, BMI and duration of disease.

Statistical differences were found between CIMT and the severity of LP. CIMT was higher in moderate and severe diseases ( $P=0.035$ ). In the subgroup analysis regarding involvement of LP, CIMT was higher in mucocutaneous type ( $70 \pm 0.12$ ) and lower in mucosal LP ( $0.65 \pm 0.16$ ). The number of atherosclerotic plaques was higher in cutaneous LP ( $P=0.152$ ) (Table 2, Figure 1,2).

## DISCUSSION

The metabolic syndrome is a factor resulting in global epidemics of cardiovascular diseases. Early identification of individuals with MS can help them to prevent the mortality and morbidity of cardiovascular diseases.

Based on the results of research, psoriasis and

**Table 1.** Demographic, clinical and laboratory characteristics of patients with lichen planus and healthy controls

	Patients with lichen planus (n=40)	Healthy controls (n=40)	P-value
Age (years)			
Mean±SD	44.2±12.4	43.1±9.2	0.656
Females/ males, n (%)	16 (40)/ 24 (60)	14 (35)/ 26 (65)	
BMI* (Kg/m <sup>2</sup> )	27.5±4.4	27.3±3.2	0.795
Diastolic blood pressure, mmHg	117±12.2	112±12.8	0.111
Systolic blood pressure, mmHg	72±10.2	69±9.3	0.231
Abdominal circumference (cm)	97.5±12.3	92.6±15	0.116
Severity of disease, n (%)			
Mild	9 (22.5)		
Moderate	19 (47.5)		
Severe	12 (30)		
Clinical type, n (%)			
Cutaneous	30 (75)		
Mucosal	2 (5)		
Mucocutaneous	8 (20)		
Duration of disease (years)	3-30		
Mean	2.98		
Lipid profile (mg/dl)			
TG	160.4±144.5	154.1±150.9	0.849
Cholesterol	182.6±39.2	177.2±36.5	0.522
LDLc	102.7±31.3	101.4±27.6	0.835
HDLc	44.2±10.3	44.3±6.7	0.928
Leptin (ng/ml)	32.6±23.2	28.7±20.3	0.429

\*Body mass index

Scoring system for lichen planus was based on the extension of skin involvement (generalized involvement; severe type, one localized involvement; mild type, others; moderate type), triglycerides (TG), low-density lipoproteins (LDL), high-density lipoproteins (HDL)

**Table 2.** CIMT and carotid plaque prevalence in patients and controls

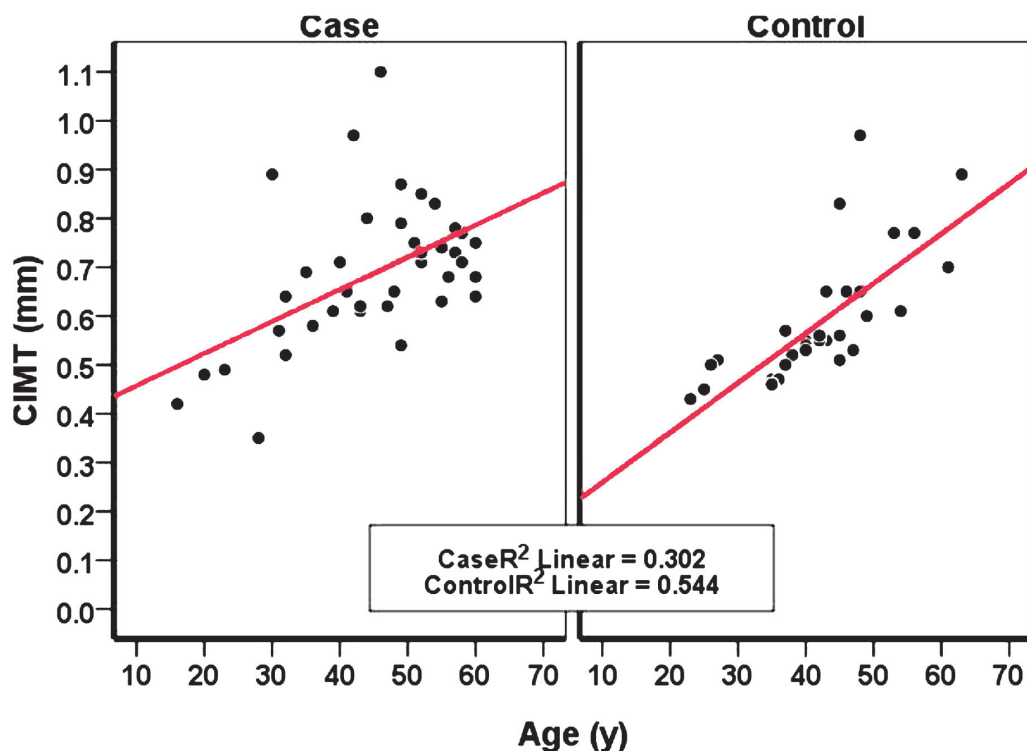
	Patients with lichen planus (n=40)	Healthy controls (n=40)	P-value
The right CIMT*, mm Mean±SD	0.67±0.15	0.59±0.12	0.012
The left CIMT, mm Mean±SD	0.69±0.16	0.59±0.13	0.005
The number of atherosclerotic plaques in CCAs#			
Right	0	0	0
Left	3	0	0.241
Severity of disease			
Mild	0.59±0.13		
Moderate and severe	0.71±0.15		0.035

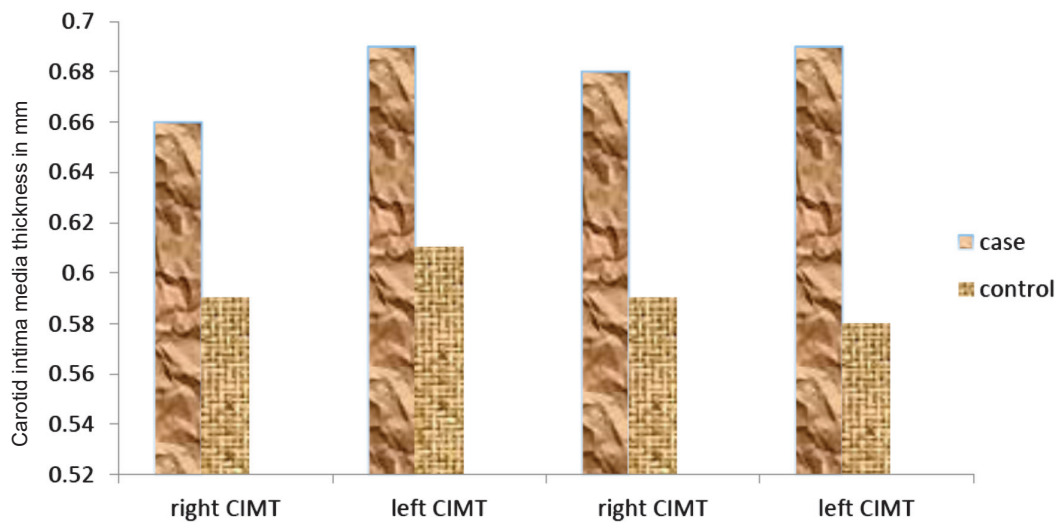
\* Carotid intima-media thickness

# Common carotid artery

cutaneous LP are associated with a significant level of risk for metabolic syndrome<sup>4</sup>. Although the exact mechanism of the relationship between cutaneous LP and metabolic syndrome is unknown, the chronic inflammation is considered the potent mechanism. Upregulation of inflammatory ligands, presence of effector cytotoxic T-cells and plasmacytoid dendritic cells<sup>5</sup>, various cytokines such as interleukins, TNF- $\alpha$ , IFN- $\alpha$ , IFN- $\gamma$  (5,6), Leptin, Adiponectin, and other Adipocytokines produced by Adipocytes<sup>7,8</sup>, oxidative stress and

a disorder in the elimination of reactive oxygen species (ROS)<sup>9-11</sup> due to the lymphocytotoxic process, play a role in the pathogenesis of LP. This chronic pro-inflammatory condition possibly can explain the correlation between LP, dyslipidemia and metabolic syndrome<sup>12</sup>. To the best of our knowledge, there are few studies on the association between dermatologic conditions and subclinical atherosclerosis. Recent studies have indicated that average CIMT values were increased in patients with LP who had no clinical evidence of heart

**Figure 1.** The correlation between CIMT and age



**Figure 2.** Carotid intima media thickness in the patients and controls

diseases<sup>13</sup>. Impaired levels of flow-mediated dilatation (FMD) and increased CIMT are the sensitive predictors of early endothelial dysfunction and structural changes in patients with LP<sup>14</sup>. The present research aimed to study the association of cutaneous LP with carotid intima-media thickness (CIMT) and the number of atherosclerotic plaques in CCAs in patients with LP not known to have CVD cardiovascular disease (CVD) risk factors and smoking habits. Although in some studies, CIMT was correlated with the longevity of LP<sup>15</sup>, others were not correlated, like ours<sup>13,14</sup>.

Carotid IMT adjusted for variables was significantly associated with the PASI score in psoriasis<sup>16</sup>.

In our study, a significant correlation was found between the severity of disease and atherosclerotic variables. According to previous studies, there was a significant correlation between age and CIMT in LP patients, like our study<sup>13,14</sup>.

The participants did not have any cardiovascular risk factors. To make conflicting factors least, we excluded individuals with smoking habits, then we could find out closely whether LP was a dependent predictor of increased CIMT.

In studies on carotid Doppler ultrasound evaluation in patients with Lichen planus, carotid plaque prevalence was not evaluated. Only Troitzsch *et al.* could demonstrate that psoriasis was associated with mean CCA-IMT, but not with carotid plaque prevalence<sup>17</sup>. We assessed the number of atherosclerotic plaques in patients

with LP, but there was no significant difference.

Our study has some limitations. The overall sample was restricted by the rigid inclusion criteria; moreover, financial constraints were another limitation.

Subclinical atherosclerosis and cardiovascular morbidity are more frequent and considerably challenging. For better prophylaxis, early diagnosis of atherosclerosis or lipid profile monitoring is important in patients with lichen planus. Measurement of the mean intima media wall thickness of the common carotid artery could be beneficial as a valuable method for the mentioned reason.

Undoubtedly, CIMT in LP is correlated with some inflammatory cytokines and complicated pathogenic and proatherogenic pathways. We suggest that future studies be conducted to clarify the connection of atherogenesis to cytokines in LP.

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**Conflict of Interest:** None declared.

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