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TITLE: Carotid Doppler ultrasound measurements in allergic rhinitis patients

AUTHORS: Pelin Zeynep BEKIN SARIKAYA, Nuray BAYAR MULUK, Burak Mustafa TAS, Selcuk

BASER, Elif ÇETINKAYA

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Carotid Doppler ultrasound measurements in allergic rhinitis patients

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ABSTRACT

Aim: We aimed to determine with carotid Doppler ultrasound (CDU) whether the increase in inflammatory cells and mediators plays a role in intima-media thickening in patients with allergic rhinitis (AR) and to correlate this with the severity of the disease.

Material and Method: In this retrospective study, CDU reports and images of allergic rhinitis patients were evaluated in Group 1 (n=16). Score for allergic rhinitis (SFAR) and blood parameters that Hemoglobin (Hb), White Blood Cells (WBC), C-Reactive Protein (CRP), sedimentation levels were noted. Control group without AR consisted of 17 patients. In both groups, the presence of plaque on common carotid artery (CCA), and internal carotid artery (ICA) and all intima-media thickness were noted by CDU.

Results: In our study, CCA intima-media thickness and ICA intima-media thickness values of the AR group were significantly higher than those in the control group bilaterally (p<0.05). In the AR group, there were positive correlations between CCA intima-media thickness and ICA intima-media thickness values (p<0.05). In the AR and control groups, there were no plaques in ICAs bilaterally. However, left CCA plaques were detected in 2 patients (12.5%) of the AR group. In the AR group, CCA and ICA intima-media thicknesses increased in older patients; and right ICA intima-media thickness values increased in males (p<0.05).

Conclusion: Allergic rhinitis is one of the most common inflammatory diseases. It is known that the increase in mediators and inflammatory cells in the body can cause atherosclerosis. It should be kept in mind that AR patients may develop early atherosclerosis and therefore an increased cardiovascular risk.

Keywords: Allergic rhinitis, CCA intima-media thickness, ICA intima-media thickness, plaque

INTRODUCTION

Allergic rhinitis (AR), one of the most common respiratory diseases in the world, is defined as an inflammatory process triggered by mediators and cytokines in the nasal mucosaca used by exposure to allergens (1). The prevalence of AR varies between 5% and 22% worldwide (2). Its prevalence is increasing, especially in societies where industrialization has increased. AR affects the quality of life and saves the way for many diseases, especially lower respiratory tract diseases (3). AR has symptoms such as sneezing, nasal itching, runny nose, and nasal congestion (4). The diagnosis of AR can be made by anamnesis, physical examination and allergy tests.

Inflammation triggered by inflammatory mediators and factors plays an important role in the etiology of atherosclerosis (5,6). Carotid Doppler Ultrasonography (CDU) is the most commonly used method to evaluate atherosclerosis of the carotid artery and intima media layer thickening (IMT), which is the precursor of atherosclerosis (7.8).

In line with these informations, we aimed to determine with CDU whether the increase in inflammatory cells and mediators plays a role in intima-media thickening in patients with AR and to correlate this with the severity of the disease.

MATERIAL AND METHOD

This retrospective study was conducted in Radiology and Otolaryngology Departments of Kırıkkale Faculty of Medicine according to the principles of Declaration of Helsinki. Carotid Doppler ultrasound records

Corresponding Author: Pelin Zeynep Bekin Sarıkaya, zeybekin@hotmail.com

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¹Department of Radiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkey

²Department of ENT, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkey

were obtained from the Kırıkkale University Faculty of Medicine Radiology Department database. Ethics committee approval was obtained from the Non-invasive Clinical Researches Ethics Committee of Kırıkkale University (Date: 29.06.2022, Decision No: 2022.06.25).

Allergic Rhinitis Group

In this retrospective study, among the allergic rhinitis patients who came to the otorhinolaryngology outpatient clinic with the symptoms of nasal congestion, sneezing, runny nose and itching, Carotid Doppler Ultrasound were performed in the same month for other reasons was detected from our hospital data system. Carotid Doppler Ultrasound reports and images of allergic rhinitis patients younger than 50 years, were screened from the PACS (Picture archiving and communication systems) and data system of our hospital from current time to January 2022. The allergic rhinitis group consisted of 16 adults. The mean age of patients in allergic group is 34.75±10.51 (range 20 to 50). Score for allergic rhinitis (SFAR) (9-11) and blood parameters that Hemoglobin (Hb), White Blood Cells (WBC), C-Reactive Protein (CRP), sedimentation levels were noted.

Control Group

The measurements of 17 patients who were not diagnosed with allergic rhinitis and had similar age andgender characteristics with the AR group, who underwent Carotid Doppler US for any reason in the radiology department, were taken. Patients who had neck surgery, and malignancy were not included. The mean age of patients in control group is 29.64±7.46 (range 21 to 44).

Exclusion Criterias

Older patient from 50 years were excluded from the study because of the possibility of risk of aging-related atheroma plaque development. Those who have had carotid surgery or neck dissection and malignant patients were not included in the study group as this may affect the measurement results.

Score for Allergic Rhinitis (SFAR)

The SFAR is a structured scoring system that includes eight questions about AR symptoms, personal and family history of allergy, and allergy testing. According to the SFAR scoring system, as stated in previous studies, patients with a total score of 7 and above are considered for the diagnosis of AR (9,10). Turkish validation was performed for SFAR (11).

Carotid Doppler Ultrasound Measurements

Carotid Doppler Ultrasound (US) was evaluated with a digital device (LOGIQ E9; GE Healthcare, Waukesha, WI) with a linear 6–9-MHz multifrequency transducer by a radiologist with 12 years of experience in Doppler

ultrasonography. Carotid Doppler US examinations were performed in a supine position. All US examinations of the left and right CCAs and ICAs were performed, including gray scale and color and pulsed Doppler ultrasound studies with using angle correction. Flow directions and whether the flow rate was normal or not were evaluated. The presence of plaque on common carotid artery (CCA), and internal carotid artery (ICA) and all intima-media thickness were noted as centimeters (cm) (12).

Statistical Analysis

SPSS for 21.0 (SPSS; IBM Inc, Chicago, IL) was used for statistical analysis. Mann Whitney U test was used for comparison between two groups. The Sperman's correlation rho efficient test was used for the correlations in the study group. Chi-square test was used to compare nominally categorized data in groups. For comparison within the same group (right and left sides of the same patient's one measurement), the non-parametric Wilcoxon signed ranks test was used because the numbers in the groups were small, did not show a normal distribution, and the p value was less than 0.05 in the Kolmogorov Smirnov test. A p value of<0.05 was considered statistically significant.

RESULTS

In the allergic rhinitis group, there were 9 (56,3 %) males and 7 (43,8 %) females; and in the control group, there were 8 (47.1%) males and 9 (52.9%) females (p=0.598, χ 2=0.279). There were no significant differences between ages of the AR and control groups (p>0.01) (**Table 1**).

In the AR group, blood parameters were as following: Hb: 14.80±1.08 gr/dL, WBC: 8125±1.87, CRP: 2.85±2.84, sedimentation rate: 12.37±7.30.

In the AR group, SFAR scores were 7.25 ± 3.31 (ranging 1.00 to 12.00).

Measurement results in the AR and control groups are shown on **Table 1**.

CCA Intima-Media Thickness

CCA intima-media thickness values of the AR group were significantly higher than those in the control group bilaterally (p<0.05) (**Table 1**).

In each of the AR and control groups separately, there were no significant differences between CCA intimamedia thicknesses on the right and left sides (p>0.05) (Table 1).

ICA Intima-Media Thickness

ICA intima-media thickness values of the AR group were significantly higher than those in the control group bilaterally (p<0.05) (**Table 1**).

In each of the AR and control groups separately, there were no significant differences between ICA intimamedia thicknesses on the right and left sides (p>0.05) (**Table 1**).

CCA Plaque

In the AR group, there were no plaques in right CCA. However left CCA fibrofatty plaque that does not cause significant stenosis, were detected in 2 (12,5 %) patients. In the control group, there were no CCA plaques bilaterally (p=0.082, χ 2: 3.033) (**Table 1**).

ICA Plaque

In the AR and control groups, there were no plaques in ICAs bilaterally.

Correlation test results in group 1 (AR) are shown on **Table 2**:

There were positive correlations between CCA intimamedia thickness, ICA intima-media thickness, and the presence of Left CCA plaques (p<0.05) (**Table 2**).

There were no significant correlations between SFAR; and blood parameters (Hb, WBC, CRP and sedimentation rate) and CCA and ICA intima-media thicknesses and left CCA plaques (p>0.05) (**Table 2**).

In older patients with AR, CCA and ICA intima-media thicknesses increased (p<0.05) (**Table 2**).

In male patients with AR, right ICA thickness values increased compared to females (p<0.05) (**Table 2**).

	Group 1 (AR) (n=16)			Group 2 (Control group) (n=17)			. p *
_	Mean	Median	Std. Dev.	Mean	Median	Std. Dev.	- P^
Age	34.75	36.5	10.51	29.64	28.00	7.46	0.213
Measurement results							
CCA intima thickness (mm)							
R	0.06	0.06	0.01	0.04	0.04	0.01	0.000
L	0.06	0.06	0.02	0.04	0.04	0.01	0.000
P**		0.974			0.166		
ICA intima thickness (mm)							
R	0.05	0.05	0.01	0.02	0.03	0.00	0.000
L	0.05	0.05	0.02	0.03	0.03	0.00	0.000
P**	0.158			0.763			
	n		%	n		%	P***
Left CCA Plaque							
Present	2		12.5	0		0.0	P=0.082
Absent	14		87.5	17		100.0	χ2: 3.033

Table 2: Correlation test results in group 1 (AR)									
		CCA intima thickness		ICA intima thickness		Left CCA Plaque (Code 1:			
		R	L	R	L	Present, Code 2: Absent)			
CCA intima thickness L	r		0.551	0.879	0.606	0.568			
	P		0.027	0.000	0.013	0.022			
	r	0.551		0.491	0.747	0.504			
	P	0.027	•	0.054	0.001	0.047			
F	r	0.879	0.491		0.709	0.563			
	P	0.000	0.054	•	0.002	0.023			
ICA intima thickness	r	0.606	0.747	0.709		0.515			
I	P	0.013	0.001	0.002	•	0.041			
Left CCA Plaque (Code 1:	r	0.568	0.504	0.563	0.515				
Present, Code 2: Absent)	P	0.022	0.047	0.023	0.041	•			
	r	0.095	0.347	-0.164	0.128	-0.103			
SFAR	P	0.726	0.188	0.544	0.636	0.703			
** 1.1. (/1*)	r	0.095	0.347	-0.164	0.128	-0.103			
Hemoglobin (gr/dL)	P	0.726	0.188	0.544	0.636	0.703			
LIDG	r	0.089	-0.186	0.109	0.170	0.288			
WBC	P	0.742	0.491	0.687	0.528	0.280			
0.1:	r	0.096	0.472	0.043	0.259	0.126			
Sedimentation rate	P	0.725	0.065	0.875	0.332	0.643			
CRP	r	0.373	0.446	0.433	0.362	0.328			
	P	0.154	0.083	0.094	0.168	0.215			
Age	r	0.705	0.510	0.626	0.617	0.452			
	P	0.002	0.044	0.009	0.011	0.079			
Gender	r	-0.253	-0.238	-0.556	-0.486	-0.333			
(Code 1: Male, Code 2: Female	e) P	0.345	0.375	0.025	0.056	0.207			
* p value shows the results of Spearman	n's correlatio	on rho efficient test							

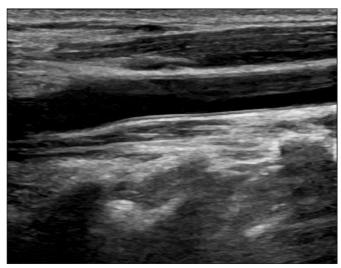


Figure 1: The figure shows the evaluation of the right common carotid artery with gray scale ultrasound.

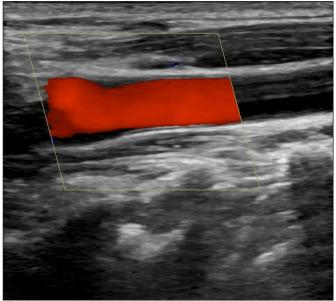


Figure 2: There is an evaluation of the flow direction in the right common carotid artery on the image.

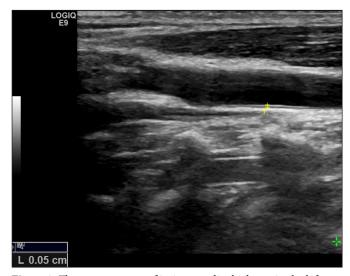


Figure 3: The measurement of intima-media thickness in the left internal carotid artery as centimeters is shown.

DISCUSSION

Allergic rhinitis is a health problem that is increasing in frequency according to recent publications and is caused by an inflammatory response to allergens (13,14). After the nasal mucosa is exposed to allergens, mast cells and basophil degranulation, immunoglobulin E production, and activation of eosinophils begin with the triggered immunomodulatory system. These are the mechanisms responsible for the clinical symptoms such as nasal congestion, sneezing, runny nose of AR (15,16).

SFAR, which was started to be used by Annesi-Maesano et al. (10) has been used for years in the diagnosis and follow-up of allergic rhinitis. AR patients were evaluated with SFAR, a score that has been validated andused in epidemiological studies (17). We aimed to obtain information about the severity of inflammation by adding SFAR results and blood values such as White Blood Cells (WBC), C-Reactive Protein (CRP), sedimentation to our study. There were nosignificant correlations between SFAR; and blood parameters (Hb, WBC, CRP and sedimentation rate) and CCA and ICA intima-media thicknesses and left CCA plagues. The reason why no significant results were obtained in this regard may be that the sample was a small group. More effective results can be obtained in larger case studies. An other reason may be that the SFAR scoring is subjective. More objective assessments are needed in this regard.

In our study, CCA intima-media thickness and ICA intima-media thickness values of the AR group were significantly higher than those in the control group bilaterally. In the AR group, there were positive correlations between CCA intima-media thickness and ICA intima-media thickness values. Moreover, in the AR group, CCA and ICA intima-media thicknesses increased in older patients; and right ICA intima-media thickness values increased in males. Looking at the literature, some studies mention that allergic diseases accelerate atherosclerosis (18,19). Although this issue has not yet been clarified, allergic disorders may be risk factors. Although allergic diseases are localized, they produce a systemic response by releasing vasoactive peptides and cytokines in to the circulation (20). Adhesion molecule expression increases not only in the nasal region, but also in distant endothelial cells. Leukocyte leakage from the endothelium increases and atherosclerosis occurs (21).

Carotid intima-media thickness is a noninvasive measurement for atherosclerosis (22). Many studies have evaluated that carotid intima-media thickness shows the risk of cardiovascular disease even in the absence of plaque (23,24). In our study, in the AR and control groups, there were no plaques in ICAs bilaterally. However, in

the AR group, there were left CCA plaque were detected in 2 (12.5%) patients. A significantly thicker IMT in the AR group may mean increased cardiovascular risk for these patients. In addition, these patients may have more plaques at advanced ages compared to the normal population. However, in the treatment of carotid plaque, questioning the presence of allergic diseases and their treatment should also take an important place.

There are also some limitations in this study. One of them is the small number of patients. Large case series are needed for better results. The presence or absence of inflammation in the body could not be excluded in the controlgroup. Further studies can contribute to the literature. Also follow-up studies are needed to demonstrate the development of atherosclerosis. Studies comparing age groups may also affect the results. Allergy tests were not performed on the patients. More meaningful results can be obtained with larger series diagnosed by allergy testing.

CONCLUSION

Allergic rhinitis is one of the most common inflammatory diseases. It is known that the increase in mediators and inflammatory cells in the body can cause atherosclerosis. It should be kept in mind that AR patients may develop early atherosclerosis and therefore an increased cardiovascular risk.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kırıkkale University Noninvasive Researches Ethics Committee (Date: 29.06.2022, Decision No: 2022.06.25).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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