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Evaluation of cardiovascular risk in people with rosacea: A prospective study

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Abstract

Systemic inflammation is accepted as a nontraditional cardiovascular risk factor and has been shown to play a role in all stages of atherosclerosis. Rosacea is a chronic inflammatory skin disease. In our study, we aimed to evaluate the cardiovascular risk in rosacea patients. 40 people with rosacea (30 women, 10 men) and a control group of 40 age- and sex-matched individuals (28 women, 12 men) who had no chronic inflammatory skin disease were included in the study. Participants' body mass index (BMI) was calculated and their blood pressure was measured. Fasting blood glucose, fasting blood insulin, lipid profile, hemogram, basic biochemical parameters, erythrocyte sedimentation rate, and C-reactive protein levels were analyzed after at least 8 hours of fasting. In all participants, carotid intima-media thickness (CIMT) was measured using high-resolution B-mode ultrasonography (with a 4 MHz linear transducer. The mean CIMT values were 0.62 (0.18) mm in the rosacea group and 0.50 (0.14) mm in the control group. Statistical comparison indicated that mean CIMT was significantly greater in the patients with rosacea compared to the control group (p=0.001). There was no significant difference between the rosacea and control groups in terms of mean height, weight, BMI, or systolic and diastolic blood pressures (p>0.05). People with rosacea should be monitored periodically in terms of cardiovascular disease risk.

Keywords: Metabolic cardiovascular syndrome, carotid intima-media thickness, rosacea

Introduction

Rosacea is a chronic inflammatory skin disease with exacerbation and remission. It affects the face to varying degrees, causing papules/pustules, erythema, and telangiectasia [1]. Although the exact molecular mechanisms remain unclear, immune system activation is thought to be primarily responsible for the pathophysiology of the disease. Regression with anti-inflammatory therapy and histopathologic findings of mixed inflammatory infiltrates also support that rosacea is a primary inflammatory disease.

Rosacea is accompanied by metabolic and endocrine diseases, cardiovascular diseases, inflammatory bowel diseases, migraine diseases, etc. [2,3].

Chronic inflammation is considered a nontraditional cardiovascular risk factor. Atherosclerosis was previously thought to occur as a result of passive lipid storage in vessel walls, but current evidence has revealed it to be a chronic process in which inflammatory cells and mediators play an important role [1]. As a chronic inflammatory skin disease, rosacea may also be associated with the risk of cardiovascular disease. There are very few studies investigating this relationship, and their results have been contradictory. In our study, we aimed to evaluate the cardiovascular risk in rosacea patients and present our findings in the context of the available literature data.

Materials and Methods

This prospective randomized controlled study included a total of 80 patients presenting to the dermatology outpatient clinic between March 2019 and April 2020: 40 people with rosacea (30 women, 10 men) and a control group of 40 age- and sex-matched individuals (28 women, 12 men) who had no chronic inflammatory skin disease and received diagnoses other than rosacea. Ethical committee approval for the study was granted by the Local Ethics Committee (2019-03/06). The informed consent form was obtained from all participants.

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Patients with known traditional cardiovascular risk factors, any systemic disease such as diabetes, hypertension, dyslipidemia, malignancy, history of trauma or surgery in the last month, smoking, or chronic dermatological diseases such as psoriasis and pregnant women were excluded from the study.

Demographic data and rosacea-related information (type, duration, and severity) were recorded, body mass index was calculated, and blood pressure was measured. In addition, fasting blood glucose, fasting blood insulin, lipid profile, hemogram, basic biochemical parameters, erythrocyte sedimentation rate, and C-reactive protein levels were analyzed after at least 8 hours of fasting. The rosacea classification and staging report of the National Rosacea Society Expert Committee was used to determine the type and severity of rosacea disease [5]. HOMA-IR (Homeostatic Model of Assessment-Insulin Resistance) score was used to evaluate insulin resistance and NCEP ATP III (National Cholesterol Education Program, Adult Treatment Panel III) criteria were used to evaluate for metabolic syndrome [6].

In all participants, carotid intima-media thickness (CIMT) was measured using high-resolution B-mode ultrasonography (Aplio 400, Toshiba Canon Medical Systems Europe B.V., Netherlands) with a 4 MHz linear transducer. The carotid arteries were examined for the presence of plaques in the transverse plane from the supraclavicular level to the mandible. The probe was then rotated 90 degrees and examination continued in the longitudinal plane. The distance between the two echogenic lines representing the lumen-intima interface and the media-adventitia interface on the posterior (far) wall of the main artery in the segment 1 cm proximal to the bifurcation was measured 3 times and the mean of these values was recorded as CIMT. Measurements were repeated for both carotid arteries. Mean CIMT was evaluated as the average of the CIMT of the right and left carotid arteries. Care was taken to obtain measurements in the late phase of the cardiac cycle. All evaluations were performed by a single radiologist who was blinded to the patients' clinical and laboratory information.

Statistics

The data were evaluated using the SPSS version 22.0 package program. Data were analyzed by Kolmogorov-Smirnov test, Mann-Whitney U test, Fisher's exact chi-square test, and correlation analysis. P values < 0.05 were considered statistically significant.

Results

The rosacea group included 10 men (25%) and 30 women (75%), while the control group included 1 2 men (30%) and 28 women (70%) (p=0.617). The mean (SD) age was 41.45 (10.35) years in the rosacea group and 43.85 (8.9) years in the control group (p=0.282). There were no significant differences between the study and control in terms of age or sex.

Rosacea subtype was papulopustular in 16 patients (40%), erythematotelangiectatic in 22 patients (55%), and phymatous in 2 patients (5%). Rosacea severity was evaluated as mild in 19 patients (47.5%), moderate in 15 (37.5%), and severe in 6 (15%). The mean (SD) CIMT values were 0.62 (0.18) mm in the rosacea group and 0.50 (0.14) mm in the control group. Statistical comparison indicated that mean CIMT was significantly greater in the patients with rosacea compared to the control (p=0.001). In addition, no statistically significant difference was found between CIMT and rosacea severity (p=0.916).

The mean (SD) waist circumference was 91.1 (11.69) cm in the rosacea group and 85.57 (8.26) cm in the control (p=0.017).

There was no significant difference between the rosacea and control groups in terms of mean height, weight, BMI, or systolic and diastolic blood pressures (p>0.05) (Table 1).

While 10 (25%) of the individuals in the rosacea group were smoking; 16 (40%) of the individuals in the control group smoked. There was no statistical difference between the groups in terms of smoking.

Table 1. Comparison of physiological and laboratory parameters between the rosacea and control groups

	Rosacea group (n=40) mean ± SD	Control group (n=40) mean ± SD	Statistics p
Height (cm)	163.50 ± 9.20	164.8 ± 8.57	p=0.51
Weight (kg)	75.15 ± 11.88	75.40±12.08	p = 0.926
Waist circumference (cm)	91.10±11.69	85.57±8.26	p=0.017
Body mass index	28.23±5.19	27.84±4.44	P=0.72
Systolic blood pressure (mmHg)	125.60±16.88	120.50±14.10	P=0.146
Diastolic blood pressure(mmHg)	84.30±11.32	80.75±8.90	0.123
Fasting blood glucose (mg/dL)	89.27±11.42	91.80±7.06	0.238
Fasting insulin (uU/mL)	9.72±6.04	9.38±4.10	0.77
Total cholesterol (mg/dL)	185.37±42.14	184.50±37.46	0.922
Triglycerides (mg/dL)	136.65±96.63	151.37±77.12	0.454
Low-density lipoproteins (mg/dL)	123.75±40.92	123.55±33.64	0.981
High-density lipoproteins (mg/dL)	50.42±13.68	45.92±13.74	0.46

There was also no statistically significant difference between the rosacea and control in terms of fasting blood glucose, fasting blood insulin, total cholesterol, LDL, or HDL (p>0.05) (Table 1). There was no statistically significant difference between the groups in HOMA-IR scores for insulin resistance (p=0.893). The rosacea and control groups also showed no difference in terms of metabolic syndrome and dyslipidemia (p=0.133, p=0.818).

Contrary to our expectation, we detected no statistically significant differences between the groups in the inflammation markers CRP and sedimentation rate (p=0.977, p=0.406).

A moderate positive correlation was observed between CIMT and waist circumference (r=0.46, p=0.003). The same relationship was observed in the control group but it was very weak and nonsignificant (r=0.25, p=0.118). CIMT and age showed a relatively stronger positive correlation in the rosacea group (r=0.64, p=0.001) and a moderate correlation in the control group (r=0.49, p=0.002). There were no other significant correlations among the studied parameters.

Discussion

Rosacea causes pronounced facial redness and therefore can impair self-esteem and quality of life [6]. The prevalence of rosacea varies between 0.09% and 22% worldwide [8].

The literature data on rosacea and cardiovascular risk are controversial. Very few studies have been conducted on this subject. Some of the case-control studies have shown that traditional cardiovascular risk factors such as metabolic syndrome, insulin resistance, hypertension, smoking or alcohol use, hyperlipidemia, and familial cardiovascular diseases are more common in people with rosacea than in those without, and this was emphasized as potentially associated with increased cardiovascular risk in rosacea [4,9,10]. Hua et al. reported an increased risk of cardiovascular disease in people with rosacea compared to the general population [9]. On the other hand, a population-based study by Egeberg et al. showed that rosacea patients did not have an increased risk of cardiovascular events such as heart attack, ischemic or hemorrhagic stroke, and cardiovascular death [10]. Similarly, Marshall et al. found no significant association between rosacea and cardiovascular risk factors or disease [11].

The most common cause of cardiovascular mortality and morbidity is atherosclerosis and the most common method used to detect subclinical atherosclerosis is the calculation of CIMT with B-mode ultrasound [12].

In a cross-sectional study to investigate subclinical atherosclerosis in rosacea patients, CIMT and epicardial fat thickness were found to be higher in rosacea patients than in the control group. [13]. However, patients with cardiovascular risk factors were also included in this study. Therefore, it is difficult to say whether the increased CIMT and epicardial fat thickness seen in the patient group was independently associated with rosacea or with concomitant traditional cardiovascular risk factors [14]. In another study, as in our study, all patients with known cardiovascular risk factors were excluded and there was no statistically significant difference between rosacea and the control in terms of CIMT [15].

In our study, we minimized the risk of bias by excluding all individuals with any known cardiovascular risk factors, and we observed thicker CIMT values in the rosacea compared to the control. In addition, in our study, CIMT increased in association with age in both the rosacea and control groups, but this correlation was stronger in the rosacea group. Taken together, the results suggest that the chronic recurrent inflammation seen in rosacea contributes to the development of subclinical atherosclerosis.

The metabolic syndrome causes various systemic disorders including insulin resistance, abdominal obesity, glucose intolerance, diabetes, dyslipidemia, hypertension, vascular inflammation, and prothrombotic states, which are also a collection of risk factors for cardiovascular disease. Belli et al. investigated MS and insulin resistance in rosacea and found that insulin resistance, blood lipids, and blood pressures were significantly higher than the control group [16]. As mentioned before, patients with traditional cardiovascular risk factors were also included in their study, which obscures the true cause of the study findings. In our study, metabolic syndrome was present in 14 (35%) of the patients with rosacea and 8 (20%) of the individuals in the control group. However, a significant increase in metabolic syndrome or insulin resistance was not detected in patients with rosacea.

Many studies have shown that adipose tissue is associated with increased waist circumference, increased insulin resistance, and inflammation and leads to various metabolic events. This relationship was demonstrated by increased hepatic glucose production (via glycogenolysis and gluconeogenesis) and insulin resistance as a result of free fatty acids, inflammatory cytokines, and specific adipokine secretions released from enlarged adipose tissue [17-20]. In our study, BMI and waist circumference were significantly higher in rosacea compared to the control, indicating greater abdominal fat deposition in patients with rosacea. Inflammatory cytokines produced due to this excess visceral adipose tissue in patients with rosacea may help to explain subclinical atherosclerosis detected in this group in our study. According to the data obtained from our study, there was a significant positive correlation between waist circumference and CIMT in both patients with rosacea and controls.

There are only a few studies in the literature that examine the relationship between rosacea and dyslipidemia. Belli et al. found that the mean total cholesterol, triglyceride, and LDL levels were significantly higher in the rosacea group [16]. Duman et al. reported that the prevalence of some cardiovascular risk factors such as high total cholesterol and LDL levels, familial cardiovascular disease, and history of smoking and alcohol use was significantly higher in the rosacea group. However, there were no significant differences in terms of low HDL, high triglycerides, fasting blood glucose, obesity, high waist circumference, and hypertension [4]. In our study, we did not detect a significant difference between the groups in terms of total cholesterol, triglyceride, LDL, HDL, or dyslipidemia.

Systemic inflammation is accepted as a nontraditional cardiovascular risk factor and plays a role in all stages of atherosclerosis, starting with initiating the atherosclerotic process by causing endothelial dysfunction [21]. Many previous studies have demonstrated increased cardiovascular risk in chronic inflammatory diseases such as rheumatoid arthritis, psoriasis

vulgaris, and hidradenitis suppurativa [22-25]. CRP is synthesized in liver hepatocytes upon induction by interleukin-6 and is an important mediator of the acute phase response. As such, CRP increases in all nonspecific inflammatory events and acts as a general indicator of inflammation [26]. Accordingly, CRP is an important inflammation marker that can be used to predict the risk of cardiovascular events, especially coronary artery disease [27]. Duman et al. reported significantly higher mean CRP levels in patients with rosacea, while in another study, no significant difference in high-sensitivity CRP levels was found between the rosacea and health control groups [4]. In our study, CRP and ESR were used as inflammation markers and neither parameter differed significantly between the groups.

Although the exclusion of patients with traditional cardiovascular risk factors increases the strength of our study, the difficulty in finding patients that met this criterion limited our sample size. Another limitation of the study was that we did not analyze diet and exercise, which are factors that may influence an individual's development of subclinical atherosclerosis. Studies utilizing different methods such as epicardial adipose tissue thickness, brachial artery flow-mediated dilation, and echocardiographic parameters will provide more detailed information about this subject. Because of the cross-sectional nature of our study, it is not possible to establish a causal relationship. Larger prospective cohort studies are needed for this purpose.

Conclusion

Our study showed that while CIMT increased with age and waist circumference in both groups, these correlations were stronger in the rosacea group. All of these findings suggest that people with rosacea should be monitored periodically in terms of cardiovascular disease risk, especially older patients and those with abdominal obesity.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
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Ethical approval
Ethics approval was obtained before the study by Local Ethics Committee (2019-03/06).

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