Brachial artery flow-mediated dilation and carotid intima-media thickness for assessment of subclinical atherosclerosis in rheumatoid arthritis

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Objective
The aim of this study was to assess subclinical atherosclerosis in rheumatoid arthritis (RA) patients using flow-mediated dilation (FMD) and carotid intima–media thickness (CIMT) and find their relation to disease activity.
Patients and methods
Totally, 30 RA patients without cardiac involvement and 10 controls were included in the study. Disease activity was evaluated using disease activity score 28 (DAS28) score. Low disease activity is defined by DAS28 of 3.2 or less, moderate disease activity as DAS28 3.3–5.3, and severe disease activity as DAS28 of 5.4 or more. Endothelial dysfunction is considered to be present when FMD on B-mode ultrasonography is below 4.5%. CIMT was calculated by measuring the greatest distance between lumen–intima and media–adventitia interface [mean value of two sides (right and left) was taken] using B-mode ultrasonography.
Results
The mean CIMT was significantly higher in the RA patients (1.8±0.2) than in healthy controls (1.5±0.1) (P=0.001). Taking the mean±SD of the control group (1.6 mm) as the upper limit of the normal CIMT, 22 (73.3%) RA patients and three (30%) controls had abnormal mean CIMT, which was statistically significant. Brachial FMD% in RA patients was significantly lower (22.9±11.0) as compared with controls (35.5±23.2) (P=0.027). A statistically significant positive correlation was observed between CIMT values of patients with age, C-reactive protein, and low-density lipoprotein. There was a significant negative correlation between CIMT and hemoglobin and brachial FMD. FMD% showed a statistically significant negative correlation with age, disease duration, low-density lipoprotein, Framingham cardiovascular risk score, and mean CIMT.
Conclusion
Carotid ultrasound and endothelial function assessment by means of FMD may be a useful tool to predict the increased risk for cardiovascular disease in patients with RA, which requires aggressive therapy.

Keywords:
carotid intima–media thickness, flow-mediated dilation, rheumatoid arthritis, subclinical atherosclerosis

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Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory, autoimmune disease of unknown origin that affects 1–2% of adult populations with characteristic persistent symmetric polyarthritis (synovitis) and extra-articular involvement of the skin, heart, lungs, and eye [1].

The systemic and articular inflammatory load drives the destructive progression of the disease, and the extent of inflammation in RA has been linked to an increased risk for cardiovascular (CV) mortality resulting from accelerated atherogenesis [2].

RA is associated with an increased CV morbidity and mortality as compared with the general population, and the reported relative risk for cardiovascular disease (CVD) in RA patients ranges from 1.5 to 4.0 [3,4]. The exact mechanism of association between RA and CVD remains unclear. Available studies indicated that adjustment for conventional cardiovascular disease risk (CVR) factors does not account for the higher rates of CV events in RA populations, suggesting that, the process of inflammation, probably the driving force for premature atherosclerosis in RA because striking parallels can be drawn between the atherosclerotic plaque and synovitis in RA at the tissue level, is an independent risk factor for CVD [5]. Besides

traditional CVR factors and chronic inflammation, recent studies have also highlighted the involvement of genetic factors and the influence of several gene polymorphisms in the risk for accelerated atherosclerosis of patients with RA [6].

Carotid B-mode ultrasound (US) is a convenient noninvasive method for detecting subclinical atherosclerosis [7]. Carotid intima–media thickness (CIMT) and the presence of plaque in the carotid arteries are strongly associated with CVR factors and generalized atherosclerosis [8,9], and are also a strong predictor of future CV events.

CIMT has been used in several clinical trials as a surrogate endpoint for evaluating the regression and/or progression of atherosclerotic CVD [10,11].

The importance of abnormally high CIMT and plaques as predictors of CV events in patients with RA has been emphasized [12,13].

The human vascular endothelium provides structural and functional roles within the body. A healthy endothelium allows for mechanical to chemical signal transduction to maintain homeostasis of the blood vessel [14]. Endothelial dysfunction is an imbalance of these mediators and the first step in vascular disease, present before histological evidence of atherosclerosis. A noninvasive, in-vivo method for quantifying the vasodilatory function of human artery exists. This method, endothelium-dependent, flow-mediated vasodilation (FMD), is widely used in clinical trials.

Importantly, endothelial dysfunction can be observed in individuals without diagnosed CVD and is predictive of future CV events [15,16,17]. Endothelial dysfunction determined by flow-mediated endothelium-dependent vasodilation (FMD) has been observed in both patients with recent onset and low disease activity as well as long-standing RA patients [18,19].

Several studies suggest that CIMT, structural measure of early atherosclerosis in RA patients and brachial artery FMD%, a physiologic measure of subclinical atherosclerosis are reliable methods to assess the subclinical atherosclerosis and may measure different stages of early atherogenesis in RA patients [20].

Aim

The aim of this study was to assess subclinical atherosclerosis in RA patients using FMD and CIMT and find their relation with disease activity.

Patients and methods

Patients

Our study was conducted in the Rheumatology Unit, Internal Medicine Department, Assiut University Hospitals, Egypt. It is a case–control study. Totally, 40 individuals were divided into two groups: the patient group and the control group. The patient group included 30 patients with RA without cardiac involvement; every patient fulfilled the 2010 ACR/EULAR Rheumatoid Arthritis Classification Criteria [21]. The control group consisted of 10 healthy individuals matched for age and sex.

Exclusion criteria

(1) Age more than 70 or less than 18 years at entry.
(2) Current pregnancy.
(3) Comorbid diseases/conditions: diabetes, obesity (BMI: ≥30), familial dyslipidemia, hypertension, coronary artery disease, cerebrovascular accident, peripheral vascular disease, hypothyroidism, renal disease (serum creatinine: ≥3.0 mg/dl or creatinine clearance: ≤30 ml/min), liver disease, and Cushing's syndrome.
(4) Concurrent treatment with lipid-lowering drugs, β-blockers, oral contraceptives, estrogens, progestin, thyroxin, and steroids.
(5) Refusal to be enrolled in the study.

Ethical considerations

Written informed consent was taken from all study participants and the study protocol was approved by the Ethical Committee of the Faculty of Medicine.

Methods

(1) Full history taking, including age, sex, duration of the disease, and type of treatment.
(2) Complete clinical examination, BMI, and joint examination, which included tender joint count (TJC), swollen joint count (SJC), and deformity. A composite disease activity score 28 (DAS28) was calculated using three variables: SJC (28), TJC (28), and Westergren's erythrocyte sedimentation rate (ESR). The low disease activity is defined by DAS28 of 3.2 or less, moderate disease activity as DAS28 3.3–5.3, and severe disease activity as DAS28 of 5.4 or more [22]. Framingham CVR score was calculated depending mainly on blood pressure (BP) and lipid profile for evaluation of risk for heart disease in 10 years [23].

(3) Laboratory investigations:
   (a) Complete blood count was performed using automated cell counter.
   (b) ESR was measured using the modified Westergren's method.
   (c) C-reactive protein (CRP) and rheumatoid factor (RF) were measured using the latex agglutination method.
   (d) Serum levels of cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were determined using a semi auto analyzer.
   (e) Blood urea and serum creatinine, fasting blood glucose, and serum uric acid were measured using the spectrophometeric method using stat fax.
   (f) Complete urine analysis was performed by means of microscopic examination.
   (g) Radiography of the hands and feet was performed to assess radiological bone and cartilage changes using van der Heijde modification of Sharp score of joint involvement by RA on plain radiographs [24].
(4) Ultrasonographic scanning of the carotid artery was performed using an echographic system to detect CIMT. CIMT was increased if it was more than 0.7 mm.
(5) Flow-mediated vasodilatation of brachial artery.

The procedure was performed by a single radiologist. The participants were asked to abstain from alcohol, caffeine, and smoking at least 8 h before the procedure. The participant was made to lie in a supine position for 10 min. The right brachial artery was scanned in longitudinal section 2–15 cm above the antecubital fossa with B-mode ultrasonography images using 7–12-MHz broadband linear array transducer. The center of the artery was identified where the clearest picture of the anterior and posterior intimal layers was available. In this suitable transducer position, which was kept constant throughout the procedure, a resting scan was obtained. The luminal diameter of the brachial artery was measured using pulsed Doppler (D1). A sphygmomanometer cuff placed around forearm distal to the scanned region was inflated to 200 mmHg for 4.5 min and then released, which induced increased flow. A second scan was taken at this stage and again luminal diameter of the artery was measured 60 s after cuff deflation (D2). Endothelial dysfunction is considered to be present when FMD is below 4.5% [25,26]. The endothelium-dependent function is defined by the following formula:

$$\frac{(D2D1)}{D1} \times 100.$$

The higher the numeric value of the study, the better is the endothelial function (Figs 1 and 2).

Statistical analysis

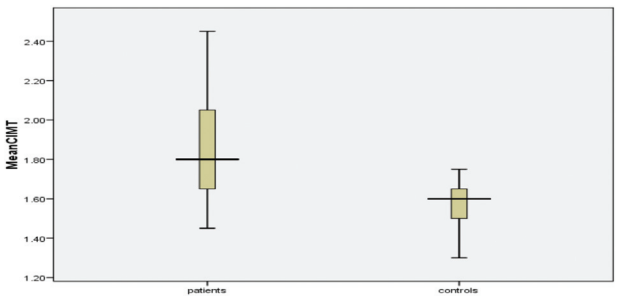
Statistical analysis was performed using statistical package for the social sciences, version 16.0, for Window software (SPSS Inc., Chicago, Illinois, USA). Mean and SDs were used to express quantitative data. For continuous variables, testing between two groups was performed using the Mann–Whitney *U*-test. Categorical variables were compared using Pearson's χ^2-test when very small proportions were analyzed. A correlation between variables was examined using the Pearson's correlation coefficient. Multiple linear regression analysis was used to explore a predictive relationship between FMD and CIMT with major variables. *P* values of less than 0.05 were considered statistically significant. *P* values of more than 0.05 were considered statistically nonsignificant.

Results

This study included 30 patients (27 women and three men) with an average age of 47.4±11.9 years and average disease duration of 9.0±5.5 years. As regards controls, there were 10 healthy controls (five women and five men)with an average age of 38.0±12.2. Twenty-five (83.3%) patients were RF positive (RF titer 121.7±127.8 IU/ml). Three (10%) patients had low DAS 28 score (2.0–3.1), 14 (46.6%) patients had moderate DAS 28 score (3.5–5.3), and 13 (43.3%) patients had high DAS28 score (Tables 1 and 2).

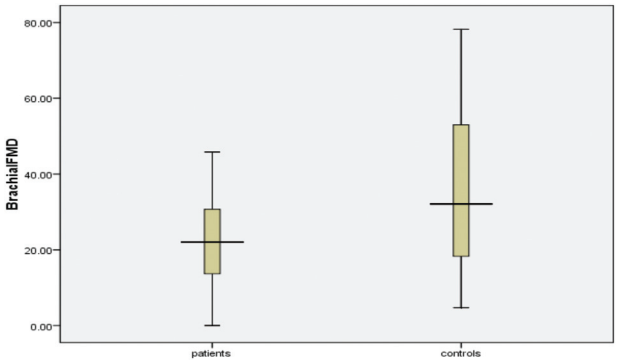
There were no significant differences between patients and controls in most clinical variables such as BP and BMI. Age and sex were significantly higher in RA patients as compared with controls (Table 1).

Figure 1



Comparison between mean carotid intima–media thickness (CIMT) of both patients and controls. As shown in this figure, the mean CIMT was significantly higher in the rheumatoid arthritis patients (1.8±0.2) than in the healthy controls (1.5±0.1; *P*=0.001). Taking the mean±SD of the control group (1.6 mm) as the upper limit of the normal CIMT, 22 (73.3%) rheumatoid arthritis patients and three (30%) controls had abnormal mean CIMT, which was statistically significant.

Figure 2



Comparison between percentages of flow-mediated vasodilatation (FMD%) of both patients and controls. As shown in this figure, brachial FMD% in rheumatoid arthritis patients was significantly lower (22.9±11.0) as compared with controls (35.5±23.2) (*P*=0.027).

On comparing laboratory and radiological findings between RA patients and controls, ESR, LDL, mean CIMT, and brachial FMD were significantly higher in RA patients as compared with the control group (Table 2 and Figs 3 and 4).

We looked for any correlation of high CIMT and low FMD% values of patients with factors such as disease duration, ESR, CRP, RF titer, Framingham CVR, and DAS28 to assess how these factors contributed to atherosclerosis in RA. A statistically significant positive correlation was observed between CIMT values of patients with age, CRP, and LDL. However, there was no significant correlation between CIMT and the other variables except hemoglobin and brachial FMD with which there was a negative correlation (Table 3).

Among the above contributing factors, FMD% showed a negative correlation with most variables as expected but the correlation was statistically significant with age, disease duration, LDL, Framingham CVR score, and mean CIMT, as shown in Table 3. Bold values are statistically significant.

Multiple regression analysis involving most clinical and laboratory features with FMD revealed disease duration, hemoglobin level, serum creatinine level, and Framingham CVR score to be significant determinants for FMD when adjusted for other independent variables. This analysis also revealed no significant factors for CIMT (Table 4).

Discussion

RA is associated with increased CV mortality as a result of accelerated atherosclerosis [2].

Table 1 Clinical data of the rheumatoid arthritis patients and healthy controls

Variables	RA patients (*n*=30)	Healthy controls (*n*=10)	*P* value
Age (years)	47.4±11.9	38.0±12.2	0.037
Sex (female/male)	27/3	5/5	**0.005**
Disease duration (years)	9.0±5.5	–	–
Morning stiffness (h)	0.79±0.87	–	–
RAI	14.6±9.2	–	–
TJC	11.3±5.8	–	–
SJC	1.8±2.3	–	–
Deformity (present/not)	11/19	–	–
BMI (kg/m^2)	25.8±4.4	24.2±4.4	0.308
Systolic BP (mmHg)	127±15.7	126±10.7	0.854
Diastolic BP (mmHg)	81±11.5	80±9.4	0.806

Data are expressed as mean±SD. Bold values are statistically significant. BP, blood pressure; RA, rheumatoid arthritis; RAI, Ritchie articular index; SJC, swollen joint count; TJC, tender joint count.

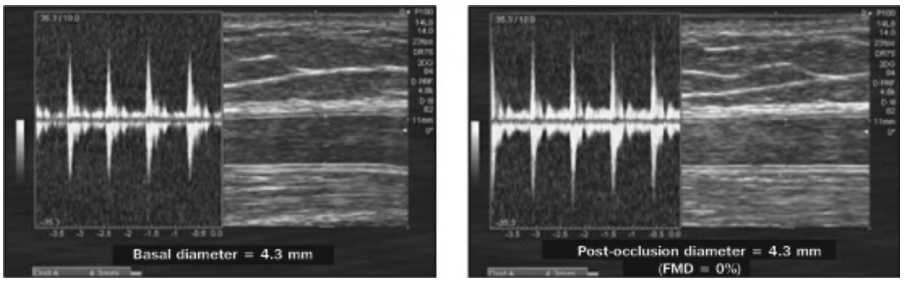
Table 2 Laboratory and radiological data of the rheumatoid arthritis patients and controls

Variables	RA patients (*n*=30)	Healthy controls (*n*=10)	*P* value
Hemoglobin (g/dl)	11.1±1.9	12.2±0.8	0.093
ESR (mm/first hour)	48.8±31.4	7.7±4.4	**0.000**
CRP (mg/l)	62.9±127	1.2±0.8	0.136
RF titer (IU/ml)	121.7±127.8	–	–
Blood urea (mmol/l)	5.3±3.5	4.9±1.2	0.727
Serum creatinine (μmol/l)	68.1±35.7	68.3±9.1	0.986
FBG (mmol/l)	5.2±1.2	5.1±0.8	0.800
Uric acid (mg/dl)	4.5±2.6	4.6±1.3	0.923
Cholesterol (mg/dl)	178.1±47.1	185.0±37.3	0.678
Triglycerides (mg/dl)	111±53.9	85.1±15.9	0.145
HDL (mg/dl)	49.8±16.4	60.3±12.4	0.076
LDL (mg/dl)	107.3±41.3	75.6±14.4	**0.024**
Framingham CVR score	6.9±6.8	3.2±3.6	0.112
DAS28	5.0±1.2	–	–
Plain radiographic hand score	121.6±40.7	–	–
Mean CIMT (mm)	1.8±0.2	1.5±0.1	**0.001**
Brachial FMD%	22.9±11.0	35.5±23.2	**0.027**

CIMT, carotid intima–media thickness; CRP, C-reactive protein; CVR, cardiovascular risk; DAS28, disease activity score 28; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; FMD, flow-mediated vasodilatation; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RA, rheumatoid arthritis; RF, rheumatoid factor. Bold value mean the significant one.

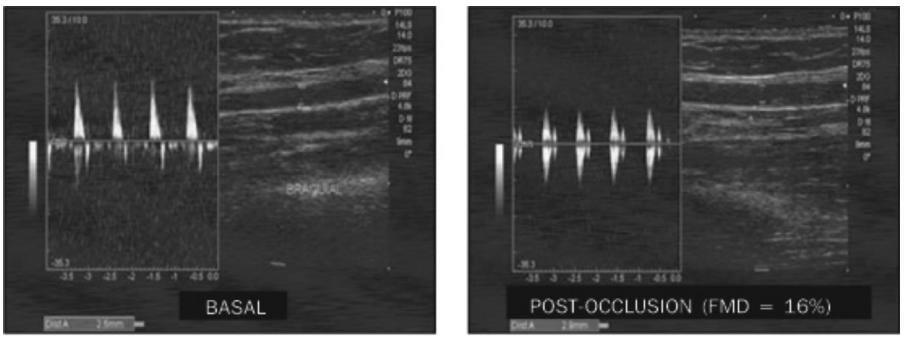
At present, several noninvasive imaging techniques offer a unique opportunity to study the relation of surrogate markers for the development of atherosclerosis. The use of these techniques may help identify high-risk individuals who may benefit from active therapy to prevent clinical disease [27].

Figure 3



FMD in a patient with RA: basal diameter=4.3 mm; post occlusion=4.3 mm; FMD=0% showing poor endothelial function, because nitric oxide production has not occurred after induction (occlusion).

Figure 4



FMD in a patient with a good endothelial function: basal diameter=2.5mm; after occlusion=2.9mm. FMD=16%.

Two important noninvasive techniques were useful in the assessment of subclinical atherosclerosis, the evaluation of endothelial function by FMD%, and the measurement of CIMT using high-resolution B-mode ultrasonography [28].

Therefore, in our study, we selected patients with RA without clinically evident CVDs. There were no significant differences between patients and controls in most clinical variables such as systolic BP, diastolic BP, and BMI. However, other clinical variables such as disease duration, morning stiffness, Ritchie articular index, TJC, SJC, and RA deformities are not correlated with the controls.

Our results show that the CIMT has a high predictive value for the development of CVD. The results implicate that the mean CIMT of the common carotid artery was significantly higher in RA patients than in healthy individuals.

Our results were the same as Gonzalez and colleagues [12,20,29,30,31,32,33], in which the presence of subclinical atherosclerosis, manifested by increased value of CIMT is consistent with the high rate of silent ischemic heart diseases and sudden cardiac death observed in RA patients and had high predictive power for the development of CVD events over a 5-year follow-up period.

Endothelial dysfunction plays a key role in early atherosclerosis and contributes to the development of clinical features in the later stages of CVD [34]. Because endothelial function in brachial circulation is correlated with endothelial function observed in coronary circulation, vascular US examination is now considered a safe noninvasive technique for examining FMD.

The results of our study show that FMD of brachial artery has a significant endothelial dysfunction in RA patients than in healthy controls. Similar to the present study, other studies such as that by Amin *et al.* [20] have found a significant endothelial dysfunction in patients with autoimmune disease such as RA by means of FMD. The presence of systemic inflammation predisposes to atherosclerosis, affecting the endothelial function and decreasing the production of nitric oxide by the endothelium; this decrease in the nitric oxide production leads to a smaller arterial dilatation upon induced ischemia [20].

Our study showed a significant correlation of CIMT and FMD in RA patients with several clinical

Table 3 Correlation of major contributing factors with carotid intima–media thickness and flow-mediated vasodilatation percentage in rheumatoid arthritis patients

Variables	CIMT		FMD	
	Correlation (*r*)	*P* value	Correlation (*r*)	*P* value
Age	0.436	**0.005**	–0.479	**0.002**
Disease duration	–0.023	0.903	–0.418	**0.021**
RAI	0.162	0.391	0.090	0.637
TJC	0.145	0.445	0.082	0.666
SJC	0.016	0.934	–0.078	0.682
BMI	–0.028	0.866	–0.074	0.650
Systolic BP	0.032	0.843	–0.305	0.056
Diastolic BP	–0.076	0.640	–0.303	0.057
Hemoglobin	–0.351	**0.027**	0.139	0.392
ESR	0.245	0.128	–0.232	0.150
CRP	0.327	**0.039**	–0.215	0.184
RF titer	0.355	0.054	–0.080	0.673
FBG	–0.060	0.715	–0.034	0.837
Uric acid	–0.202	0.210	–0.243	0.131
Cholesterol	–0.013	0.939	–0.256	0.110
Triglycerides	0.037	0.820	–0.253	0.115
HDL	–0.301	0.059	0.122	0.455
LDL	0.345	**0.029**	–0.385	**0.014**
Framingham CVR	0.181	0.263	–0.412	**0.008**
DAS28	0.068	0.720	0.048	0.800
Plain radiographic hand score (%)	0.285	0.126	–0.166	0.381
Mean CIMT (mm)	1	–	–0.0312	**0.050**
Brachial FMD %	–0.312	**0.050**	1	–

BP, blood pressure; CIMT, carotid intima–media thickness; CRP, C-reactive protein; CVR, cardiovascular risk; DAS28, disease activity score 28; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; FMD, flow-mediated vasodilatation; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RAI, Ritchie articular index; RF, rheumatoid factor; SJC, swollen joint count; TJC, tender joint count. Bold value mean the significant one.

Table 4 Multiple linear regression analysis of carotid intima–media thickness and flow-mediated vasodilatation with major contributing factors

Variables	CIMT		FMD	
	β	Significance	β	Significance
Age	0.602	0.325	–0.602	0.124
Sex	–0.154	0.747	–0.668	0.076
Disease duration	–0.318	0.604	–0.919	**0.026**
RAI	0.401	0.700	–1.114	0.149
TJC	–0.914	0.540	0.530	0.568
SJC	0.304	0.570	–0.040	0.906
BMI	0.909	0.184	0.592	0.098
Systolic BP	–0.581	0.361	–0.130	0.771
Diastolic BP	–0.179	0.787	–0.567	0.134
Hemoglobin	–0.270	0.757	1.566	**0.032**
ESR	–0.411	0.688	0.438	0.529
CRP	0.701	0.189	0.054	0.861
RF titer	–0.013	0.970	0.192	0.344
Blood urea	0.407	0.765	–1.373	0.149
Serum creatinine	–0.732	0.729	3.717	**0.027**
FBG	0.336	0.541	–0.450	0.198
Uric acid	–0.283	0.879	–2.735	0.064
Cholesterol	0.562	0.405	0.112	0.785
Triglycerides	0.398	0.722	–0.864	0.212
HDL	–0.571	0.159	–0.099	0.674
LDL	–0.042	0.955	–0.959	0.068
Framingham CVR score	–0.517	0.693	2.305	**0.020**
DAS28	0.617	0.674	1.109	0.256
Plain radiographic hand score (%)	0.080	0.898	0.834	0.089

BP, blood pressure; CIMT, carotid intima–media thickness; CRP, C-reactive protein; CVR, cardiovascular risk; DAS28, disease activity score 28; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; FMD, flow-mediated vasodilatation; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RAI, Ritchie articular index; RF, rheumatoid factor; SJC, swollen joint count; TJC, tender joint count. Bold value mean the significant one.

variables such as age of the patient. There was a significant positive correlation with CIMT and a significant negative correlation with FMD. Disease duration has a significant negative correlation with FMD.

Our results are similar to other studies worldwide, which reported that, on multivariate analysis, only age and disease duration were found to have a significant correlation with CIMT [35,36]. Moreover, Fan *et al.* [29] confirmed our results and stated that, on the univariate analysis, a significantly positive correlation was observed between CIMT and age of the patients, disease duration, DAS, CRP, and systolic BP and a statistically inverse correlation was observed between CIMT and HDL cholesterol [29]. Adhikari *et al.* [31] supported our results and stated that age, systolic BP, TJC, and SJC had significant correlations with patient's CIMT.

Our study does not coincide with that of Schroeder *et al.* [37], in which the age of the patient does not affect the endothelial function evaluation with FMD.

Our results showed significantly higher differences between RA patients and controls in ESR level but CRP level showed no significance. CRP showed a significant positive correlation with CIMT only. Castro *et al.* [38] demonstrates that patients with RA present endothelial dysfunction, and FMD does not correlate with CRP, patient's age, and disease duration.

No significant correlation of CIMT and ESR or DAS28 was found in our study. It might be due to the fact that DAS28 and ESR levels often fluctuate in chronic inflammatory diseases, and their measurement at a single point only can show the inflammatory burden at that point of time and fails to reveal the inflammatory burden of the entire disease duration.

The same finding was also observed in previous studies [39,40,41].

In our study, Framingham CVR score showed a significant negative correlation with FMD. However, there was no significant difference between RA patients and controls.

In our study, the mean CIMT had a significant negative correlation with brachial FMD. This may be attributed to the techniques used in making the measurements of FMD% and CIMT. However, both CIMT and endothelial function measurements were performed by the same experienced radiologist and following common standardized protocols, which suggest that our techniques of measurements are accurate. Therefore, we believe that our findings support the other possibility that, in RA patients with relatively few risk factors, CIMT and brachial artery FMD% provide independent information about the atherosclerotic process. Furthermore, previous studies in patients with CVD indicate an inverse correlation between CIMT and brachial FMD [20]. These findings are also in agreement with Fan *et al.* [29], who stated that there is no correlation between measurements of CIMT and brachial artery FMD% in RA patient cohort without CVD and with relatively few risk factors. Moreover, they reported that atherosclerosis is a complex disease and may have complex pathways. Thus, both endothelial dysfunction and intima–media thickness may be stages in the pathogenesis of atherosclerosis but they are in different pathways, all of which lead to clinical CVD [29].

Lipid levels appear to be altered as a result of RA disease activity. In our study, LDL only had higher significance in RA patients than in healthy controls, whereas other parameters including total cholesterol, triglycerides, and HDL are not significant. Moreover, LDL only showed a significant positive correlation with CIMT and a negative correlation with FMD.

In previous studies, data on total cholesterol and LDL cholesterol levels in patients with RA are conflicting: some studies demonstrate similar [42] or lower [43] levels of total cholesterol, whereas others demonstrate increased levels of total cholesterol and LDL cholesterol in patients with early inactive RA [44].

Although reports on lipid profiles in RA patients vary, growing evidence suggests that patients with untreated RA have reduced total cholesterol, LDL cholesterol, and HDL cholesterol levels [45]. Regardless of the total cholesterol changes in RA patients, several studies support the notion that RA leads to a more atherogenic lipid profile (ratio of total cholesterol to HDL cholesterol), which is correlated with disease activity and improves after treatment with antirheumatic medications [46].

In our study, multiple regression analysis involving most clinical and laboratory features with FMD revealed that disease duration, hemoglobin level, serum creatinine level, and Framingham CVR score were significant determinants for FMD when adjusted for other independent variables. This analysis also revealed no significant factors for CIMT.

Quyyumi [47] affirms that systemic inflammation markers such as FMD and CIMT arise as a method for evaluating the atherosclerosis risk. He recommends the inclusion of these methods in randomized study for screening and diagnosis of CVR. Considering that a high level of systemic inflammation affects the endothelial function, inflammation markers such as FMD may provide a better evaluation for the CVR in patients with RA [47].

Therefore, in our study we demonstrate that the FMD and CIMT are promising methods for the evaluation of RA and are very helpful for the prevention of vascular risk.

Conclusion

The results from the present study support the use of carotid US and endothelial function assessment by means of FMD as a useful tool to predict the increased risk for CVD in patients with RA. We suggest that the carotid artery US should be performed for all patients with RA to establish the risk for CV complication, which requires more aggressive therapy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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