Research Article

Correlation of carotid intimal media thickness with activity and duration of Rheumatoid arthritis using carotid Doppler Ultrasonography

P. Shravan Kumar[1], Bhargavi M[2], Abhilash T[3], Mythili L[4]

[1]Dr. P. Shravan Kumar, Associate Professor, [2]Dr. Bhargavi M, Assistant Professor, [3]Dr. Abhilash T, Senior Resident, [4]Dr. Lakshmi Mythili, Senior Resident; all authors are affiliated with upgraded Department of Medicine, Osmania Medical College, Hyderabad., India.

Address for Correspondence: P. Shravan Kumar, Professor, Upgraded Department of Medicine, Osmania Medical College, Hyderabad. E-Mail:peddametlashravan@gmail.com

Abstract

Background: Cardiovascular cause is the leading cause of mortality in RA and this has been attributed to accelerated atherosclerosis. Indirect evidence of accelerated atherosclerosis in RA comes from studies using carotid artery intima media thickness (CIMT) as a marker of atherosclerotic burden and cardiovascular risk. **Aims:** To assess carotid intima-media thickness in patients with rheumatoid arthritis by using Doppler ultrasound and to study the correlation between carotid intima-media thickness and the duration and severity of rheumatoid arthritis. **Materials and Methods:** A total of 30 rheumatoid arthritis patients were enrolled during 2 year study. Patients satisfying the modified American Rheumatology Association criteria (1987) were included. Those with hypertension, cardiac disease, and diabetes mellitus were excluded. Subjects were divided into three groups (each group consist of 10 patients) based on disease duration. For measurement of carotid intimal medial thickness B-mode USG scan using 7.5 MHz probe is used. **Results:** The mean value of common carotid intima media thickness (CCIMT) was significantly higher in the study group (0.8 mm) when compared to control group (0.59 mm) (p value < 0.001). Total carotid intima media thickness (i.e., mean of total CIMT of CCA, ICA, and ECA) was significantly higher in the study group (0.76 mm) when compared to control group (0.57mm) (p value < 0.001). **Conclusion:** The study shows a significant directly proportional relation between carotid intima media thickness to longer duration of disease.

Key words: Rheumatoid arthritis, Atherosclerosis, Carotid intimal medial thickness

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder involving the joints (nonsuppurative proliferative synovitis) along with other organ involvement including blood vessels and heart [1]. Cardiovascular cause is the leading cause of mortality in RA [2]. This increased cardiovascular risk in RA patients has been attributed to accelerated atherosclerosis which has been found to be independent of the traditional risk factors [3]. Indirect evidence of accelerated atherosclerosis in RA comes from studies using carotid artery intima media thickness (CIMT) as a marker of atherosclerotic burden and cardiovascular risk [4,5]. CIMT measurement is a noninvasive and economical test which is quite reliable and sensitive for assessment of atherosclerosis [6].

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Methodology

A total of 30 rheumatoid arthritis patients were enrolled and were compared with 30 age and sex matched control subjects. Total duration of the study was 2 years. The patients included as subjects were divided into three groups (often subjects each) based on duration of disease. These were:

Group I – those subjects who had RA of less than two years (<2years)

Group II – those subjects who had RA between two to five years (2-5years)

Group III – those subjects who had RA more than five years (>5years)

After clinical evaluation and laboratory investigations, those patients satisfying the modified American Rheumatology Association criteria (1987) [7] were included in the study. Age and sex matched controls were selected from medical OPD who came for routine health check up or had non specific complaints. After taking care to exclude those suffering from hypertension, cardiac disease, and diabetes mellitus, those suffering from congenital heart disease, ischemic heart disease, valvular heart disease with rheumatic history, and diabetes mellitus, were excluded from the study. Detailed history and physical examination was taken from each patient. A simplified 28 joint articular index as described by Fuch's et al was used to assess disease activity. Twenty-eight joints included 10 proximal interphalangeal joints of the fingers, 10 metacarpophalangeal joints, and the wrist, elbow, shoulder and the knee joints bilaterally. The investigations included erythrocyte sedimentation rate (ESR), rheumatoid factor (IgG), C-reactive protein (CRP), Hemoglobin estimation, blood urea, serum creatinine, and blood sugar estimation were done. X-ray of both hands was taken in all patients to evaluate for rheumatoid activity, deformities and erosions. For measurement of carotid intimal medial thickness B-mode USG scan using 7.5 MHz probe is used and whenever required to see plaques, plaque ulceration, lumen stenosis Colour Doppler scan is used. All measurements were taken in diastole, measured in the phase when the lumen diameter is at its smallest and IMT at its largest. All subjects included in the study were evaluated for their disease activity using DAS 28 (disease activity score).

DAS 28 = 0.56√TJC + 0.28√SJC + 0.70 (logESR) + 0.014 GH

where,

TJC is tender joint count

SJC is swollen joint count

ESR is erythrocyte sedimentation rate

GH is general health status as assessed by patient on visual analogue scale (VAS).[8]

Results

The study group included 23 females and 7 males. The age and sex distribution of patients with RA is shown in Table 1. Equal number of age and sex matched controls were taken.

Table-1: Age and Sex distribution group wise.

Age groups	No. of cases	Females	Males
21-30	3	3	0
31-40	9	8	1
41-50	15	10	5
51-60	2	1	1
61-70	1	1	0
Total	**30**	**23**	**7**

The mean duration of illness in group 1 was 1 ± 0.47 years. The mean duration of illness in group 2 was 3.35 ± 0.65years. The mean duration of illness in group 3 was 11.6 ± 3.68 years as shown in table 2.

Table-2: Mean duration of disease.

Groups	Duration (years)
Group 1	1 ± 047
Group 2	3.35 ± 0.65
Group 3	11.6 ± 3.68

The groups were compared for various atherogenic biochemical risk indices. All groups were comparable – including the mean values of blood sugar and lipid profile as shown in table 3.

Table-3: Comparison of Biochemical parameters.

Biochemical parameters	Group 1	Group 2	Group 3
Blood sugar (mg%)	96	92	83
Triglycerides	150	155	148
Cholesterol	141	154	162
HDL	48	42	40
LDL	90	85	83
VLDL	30	36	41

On investigations the hemoglobin levels ranged from 9.5 to 13.5 gm% . The mean ESR in the study group was 33.1 and ranged from 10 mm to 80 mm/hour and in the control subjects the levels ranged from 10 to 40 mm/hour, with a mean of 24 mm/hour. Twenty-two patients were found to be rheumatoid factor (RF) positive. Twenty-four patients were found to have CRP >6µg/L. The disease activity, as per DAS 28, was comparable in all three groups (p value > 0.05). Although the mean values of DAS 28 were comparable across all the groups but on further subdivision, i.e., Group I – mild disease (DAS 28 = 2.6 - 3.2); group II – moderate disease (DAS 28 > 3.2 - 5.1) and group III – severe (DAS 28 > 5.1). These groups were not comparable in number (Table 4).

Table-4: Comparison of DAS28 Score in 3 groups.

	Duration(yrs)	Mean DAS28-Score	Range	<3.2	3.2-5.1	>5.1
Group 1	1 ± 047	4.485	2.54-6.83	3	3	4
Group 2	3.35 ± 0.65	4.609	2.34-6.89	2	4	4
Group 3	11.6 ± 3.68	4.657	2.47-6.77	2	5	3

The mean value of common carotid intima media thickness (CCIMT) and total carotid intima media thickness (i.e., mean of total CIMT of CCA, ICA, and ECA) were significantly higher in the study group when compared to control group (p value < 0.001) (Table 5).

Table-5: Comparison CIMT & TCIMT in study and control groups.

IMT(in mm)	Study group	Control Group	Pvalue
CCMIT	0.8	0.59	<0.001
Total CIMT	0.76	0.57	<0.001

Common carotid IMT (CCIMT) The CCIMT ranged from minimum of 0.56 mm to maximum of 1.4 mm, the mean value of group I as 0.703 ± 0.09mm; of group II was 0.791 ± 0.146 mm and of group III was 0.91 ± 0.136 mm, the increase in CCIMT with duration was significant (p value <0.001) as shown in table 6.

Table-6: Comparison of CCIMT & TCIMT with the duration of disease.

	CCIMT		TCIMT	
	Mean	Range	Mean	Range
Group 1	0.703	0.56-094	0.678	0.53-0.89
Group 2	0.79	0.58-1.1	0.74	0.54-1.03
Group 3	0.903	0.68-1.4	0.85	0.64-1.25

Based on DAS 28 i.e., disease activity score, each group was further studied as group A (2.6 - 3.1); group B (> 3.2 to 5.1) and group C (> 5.1). In these sub-groups the relationship of activity of RA with intima media thickness of carotids was studied. On comparison of various sub-groups A, B, and C to each other, the CCIMT and TCIMT were found to be statistically non-significant (p value > 0.05 in each).

Discussion

RA and atherosclerosis are associated with elevated levels of acute phase reactants – C-reactive protein (CRP), serum amyloid A, erythrocyte sedimentation rate (ESR), fibrinogen, and secondary phospholipase 2 [9,10]. The accelerated atherosclerosis has been reported in RA to be independent of traditional risk factors. According to Homa *et al*, the intima media thickness of common carotid artery (measured at areas devoid of plaque) increases linearly with age from 0.48 mm at 40 years of age to 1.02 mm at 100 years of age (following a formula 0.009 x age + 0.116mm) [11].

The mean age of the present study (including control group) was 43.4 years. So expected common carotid thickness was approximately 0.521 mm. In the present study, common carotid intima media thickness (CCIMT) in the control group was 0.591 ± 0.113 mm (almost nearing the homa equation, i.e., 0.521 mm) whereas the common carotid intima media thickness in RA was higher, i.e., 0.798 ± 0.19 mm with p value of < 0.001. The mean of total carotid intima media thickness in RA study group was 0.798 ± 0.19 mm when compared to the control group, i.e., 0.586 ± 0.104 mm (p value <0.001). A similar observation has also been shown by Gonzalez *et al* and Alkabbi *et al* in their respective studies. [12,13]. The mean common carotid IMT was significantly higher in group III (disease > 10 years) when compared to group I and II (p value < 0.001), thus suggesting that CIMT is proportional to disease duration. Gonzalez *et al* found that disease duration is one of the best predictors for the development of severe morphologic expression of atherosclerotic disease. Del Rincon *et a*l and Mahajan *et al* also had similar observations [14]. This may be due to more years of exposure to increased inflammation, and other factors like increased arterial stiffness and prothrombotic marker in RA patients [15]. Role of inflammation as a basic pathogenic mechanism in atherosclerosis is well known.

Shared immunological disease mechanisms in systemic autoimmune disorders and coronary vascular disease such as clonally expanded CD4+ and CD28 T-cells, systemic endothelial activation and circulating immune complexes, may be involved in the development of cardiovascular comorbidities in RA patients [16,17,18]. The presence of decreased insulin sensitivity and increased ceruloplasmin levels (antioxidant factor) have been attributed to atherosclerosis in RA [19].

Conclusion

This study shows a significant directly proportional relation between carotid intima media thickness to longer duration of disease. This study did not show significant relationship between activity of disease and carotid intima media thickness.

Limitations: One of the limitations of this study is that it is cross-sectional. It would be worthwhile to follow up these patients over a period of time to look for clinical events like myocardial infarction etc. Another lacuna is our inability to comment on the influence of drugs. Almost all the patients of RA were on methotrexate and the vast majority had received corticosteroids at some point of time in their disease course in varying doses for variable periods of time.

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Abbreviations: RA-rheumatoid arthritis, CIMT-carotid intimal medial thickness, CCIMT-Common carotid intimal medial thickness, TCIMT-Total carotid intimal medial thickness, DAS-Disease activity score, ECA-External carotid artery, ICA-Internal carotid artery, CCA-Common carotid artery.

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