Original Research Article

Carotid Intima-Media Thickness: An Index Early Detection of Subclinical Atherosclerosis in Rheumatoid Arthritis

Hrishikesh Shivakumar[1], Madhu G[2],Anugraha Durairaj[3*], Shilpa TA[4]

[1]Post Graduate, Department of Medicine, BMCRI, Bangalore, Karnataka, India
[2]Post Graduate, Department of Medicine, BMCRI, Bangalore, Karnataka, India
[3]Post Graduate, Department of Medicine, BMCRI, Bangalore, Karnataka, India
[4]Post Graduate, Department of Medicine, BMCRI, Bangalore, Karnataka, India

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Abstract

Background: Increased cardiovascular risk has been observed in patients with rheumatoid arthritis due to accelerated atherosclerosis. The significance of Carotid Intima-Media thickness as a surrogate marker for detecting subclinical atherosclerosis is uncertain.**Objective:** To assess the carotid intima-medial thickness (CIMT) in rheumatoid arthritis patients and to correlate it with the prognostic outcome of patients with rheumatoid arthritis(RA)**Methods:** In this cross-sectional study, 50 patients diagnosed with Rheumatoid arthritis (according to ACR-EULAR criteria)who presented to the hospital were recruited. Ultrasound B-mode examination of carotids and carotid intimamedial thickness measurement(CIMT) was carried out in these patients. Statistical software SPSS-15.0 was used for the analysis of the data. Descriptive and inferential statistical analysis was carried out.**Results**: Out of total 50 patients, 31 females (62%) and 19 patients males (38%), a total of 30(60%) had atherosclerotic changes on CIMT. These included 19 females(63.3%) and 11 males(36%). In female sub-group, atherosclerotic changes in left common carotid artery (68%) were predominant and right common carotid artery in male sub-group(64%). In case of atherosclerotic right common carotid artery(CCA) mean PSV, mean EDV and ,mean RI were found to be 55.48±9.37, 15.36±3.66 and 0.64±0.07 and in the left CCA, mean PSV, mean EDV and mean RI were 59.44±6.98, 16.80±4.48 and 0.64±0.08 respectively.EDV was found to be statistically significantly altered. There was no significant correlation between Doppler velocities in both right carotid and left carotid with Gender or age.**Conclusion**: Based on the findings of the study, it can be concluded that CIMT screening by B-mode Doppler USG scan is a useful surrogate marker for assessing subclinical atherosclerosis in patients with RA.

Keywords: Rheumatoid arthritis; CIMT; atherosclerosis

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease of marked by symmetric, peripheral polyarthritis affecting 0.5% to 1% of the general population worldwide, resulting from abnormal immune responses. It is also associated with a wide variety of extra-articular manifestation.Rheumatoid factor (RF) is the IgM antibody directed against Fc fragment of Immunoglobulin G(IgG) ,which along with the formation of immune complexes that fix complement contributes to extra-articular findings.Detailed immunogenetic studies have proven the roles of small molecule mediators of inflammation(e.g., arachidonic acid metabolites), autoantibodies, cytokines, growth factors, chemokines, adhesion molecules, and matrix metalloproteinases (MMPs) in the pathogenesis of RA and its extra-articular manifestions[1].The most common cause of death in patients with RA is cardiovascular disease. The incidence of coronary artery disease and carotid atherosclerosis is higher in RA patients than in the general population, the presence of elevated serum inflammatory markers conferring an increased risk of cardiovascular disease [2].

**Correspondence*
Dr.Anugraha Durairaj
Post Graduate,Department of Medicine,
BMCRI, Bangalore, Karnataka, India.
E-mail: anugraha.1992@gmail.com

This emphasises on the need for detailed studies of the properties of arteries and atherosclerosis in RA . Carotid artery intima-medial thickness (CIMT) is a reliable, simple and noninvasive marker of subclinical atherosclerosis. [3]Literature pertaining to such studies are not in abundance in India. Hence this study was undertaken to find out effects of Rheumatoid arthritis on Carotid intima-media thickness.

Methods

The cross-sectional study was conducted on Patients attending to the Medicine Department in hospitals attached to Bangalore Medical College and Research Institute, Bangalore during study period of October 2013 to September 2015, after obtaining informed consent for the same. 50 patients diagnosed with Rheumatoid Arthritis according to the American College of Rheumatology and the European League Against Rheumatism (ACR-EULAR) revised criteria 2010 were included in the study. Patients with Hypertension, Diabetes mellitus, Smoking, Peripheral Vascular Disease, Cerebrovascular disease and Dyslipidemia were excluded from the study. Routine blood investigations and other relevant investigations were done. They were subjected to USG B MODE Doppler of the carotids. Intima-media thickness measurements were obtained at the near or far wall of the Common Carotid Artery(CCA), bulb, Internal Carotid Artery(ICA), External Carotid Artery(ECA), and Vertebral Artery(VA) in gray-scale imaging Doppler USG. At least three Measurements of IMT were performed within a region free of plaques. The maximum IMT value was selected for each angle. An IMT superior to 1 mm was considered to be an abnormal finding.

The velocity of blood flow in these arteries were measured and expressed as PSV(Peak Systolic velocity), EDV(End diastolic velocity) and RI(Resistive Index). Ethical Commitee clearance was obtained from the college. Statistical analysis was done using Statistical software SPSS 15.0. Descriptive and inferential statistical analysis were carried out.

Results

Out of total 50 patients the minimum age of the patient was 30 years and maximum age was 70 years. Majority of the patients belonged to age group 41-50 years(40%)

Table 1: Age distribution of patients studied

Age in years	Gender		Total
	Female	Male	
30-40	10(32.3%)	4(21.1%)	14(28%)
41-50	12(38.7%)	8(42.1%)	20(40%)
51-60	6(19.4%)	7(36.8%)	13(26%)
61-70	3(9.7%)	0(0%)	3(6%)
Total	31(100%)	19(100%)	50(100%)

It was observed that Out of 50 patients 31 patients were females (62%) and 19 patients were males (38%). In the female group majority of the patients (38.7%) patients had ACR-EULAR score of 9, but in the male patients group majority of them had score of 7.

In our study 30(60%) out of total 50 patients had atherosclerotic changes of CIMT and 20 (40%) patients were found to be normal.(Table 2) The 30 patients with atherosclerotic CIMT included 19 females (63.3%) and 11 males (36%)

Table 2: Impression of patients studied

Impression	No. of patients	%
Normal	20	40.0
Atherosclerotic CIMT	30	60.0
Total	50	100.0

Among the 19 Females who had increased CIMT thickness, majority had Left Common Carotid artery involvement(13 out of 19) and among the 11 males, right common carotid was commonly involved(7 out of 11)

On trying to correlate the duration of illness with incidence of CIMT atherosclerosis (**Table 3),** patients as early as 6 months of duration of RA illness were found to have thickened CIMT , although it was not found to be statistically significant(P-value 0.751)

Table 3: Duration of Illness in relation to impression

Duration of Illness	Impression		Total
	Normal	Athero+	
1-6	4(20%)	3(10%)	7(14%)
6-12	9(45%)	14(46.7%)	23(46%)
12-24	5(25%)	6(20%)	11(22%)
24-48	2(10%)	6(20%)	8(16%)
>48	0(0%)	1(3.3%)	1(2%)
Total	20(100%)	30(100%)	50(100%)

There was insignificant correlation between age group of the patients and thickened CIMT (P-value- 0.140) or gender(P value- 0.812) The maximum number of RA patients with thickened CIMT belonged to 41-50 years age group.In patients with atherosclerotic CIMT, average PSV was found to be 55.48+/- 9.37 and average EDV was 15.36+/- 3.66 with a significant p value and RI was 0.64+/- 0.07.(TABLE 4)In case of Left CCA atherosclerotic CIMT group average PSV was 60.49+/- 7.77 and average EDV was 18.86+/- 4.52 with significant p-value and average RI was 0.65+/- 0.07.(TABLE 4)

Table 4: CCA in relation to findings of Impression

Left CCA	Impression		Total	P value
	Normal	Athero+		
PSV	57.87±5.40	60.49±7.77	59.44±6.98	0.197
EDV	13.72±2.00	18.86±4.52	16.80±4.48	**<0.001***
RI	0.63±0.09	0.65±0.07	0.64±0.08	0.261
Right CCA	**Impression**		**Total**	**P value**
	Normal	**Athero+**		
PSV	53.38±6.19	55.48±9.37	54.64±8.24	0.382
EDV	12.62±1.40	15.36±3.66	14.26±3.25	0.003**
RI	0.62±0.10	0.64±0.07	0.64±0.08	0.439

There was no significant correlation between Doppler velocities in both right carotid and left carotid with Gender indicating it to be insignificant.

Discussion

Inflammation, increased levels of homocysteine, homoeostatic imbalance, decreased mobility, low levels of antioxidants, side-effects of medication, and dyslipidaemia have been attributed to cause accelerated atherosclerosis in RA. Amongst the above causes, inflammation has the strongest association with increased atherosclerosis in RA**.**Atherosclerosis,the precursor of cardiovascular events,keeps progressing insidiously without symptoms, afflicting large sections of arterial tree including carotid and coronary arteries.The amount of lesion in the common carotid artery (CCA)can be correlating with the extent of a CIMT is a reliable marker for coronary atherosclerosis and peripheral vascular disease[4]. In 2002, Belhassen et al[5] in a pilot study reported the

value of CIMT and aortic intima-media thickness in ruling out significant CAD in patients awaiting heart valve surgery.

Atherosclerosis is observed to be more or less present equally in the coronary, cerebral, and carotid arteries**.**Assessing CIMT by USG Doppler is a non-invasive ,easily accessible such method of detecting subclinical atherosclerosis.[6]A few studies including that by Kobayashi H[7] et al and Chung[8] et al showed a higher prevalence and higher severity of atherosclerosis in the bulb-ICA in Rheumatoid arthritis. Carotti M et al [9] also found a significantly higher CIMT in RA patients . Delricon et al[10]and Mahajan et al [11]also conducted a study that reported that RA patients had significantly greater CIMT values than age-sex-matched controls, indicating the association of RA with premature atherosclerosis also reported similar observations.A recent study by Madhuri et al[12] reported relation of the CIMT with age and found a significant association between advancing age and CIMT. However in our study there was no significant correlation between Age and CIMT. It was also shown in our study that EDV was statistically significantly altered in patients with atherosclerosis. Upto 46.7% of the patients with thickened CIMT were diagnosed to have atherosclerosis even as early as 6-12 months in spite of dyslipidemia being ruled out.In conclusion, CIMT could be used also as one of the early markers of atherosclerosis and identifying such patients helping reduce cardiovascular mortality- the most common cause of death in patients with RA. CIMT measurement is a safe, inexpensive, reproducible and cost effective strategy for early detection of atherosclerosis. Overall, the prevention of the same requires a combined approach**.** The limitations of the study include short sample size and no long term follow up of patients.

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