Original article

Carotid atherosclerosis in patients with rheumatoid arthritis and rheumatoid nodules

Dionicio Angel Galarza-Delgado a, c,*, Jorge Antonio Esquivel-Valerio a, c, Mario Alberto Garza-Elizondo a, Fernando Góngora-Rivera b, c, Jorge Luis Muñoz-De Hoyos a, Griselda Serna-Peña c

a Rheumatology Service, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico
b Neurology Service, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico
c Internal Medicine Service, Hospital Universitario “Dr. José Eleuterio González”, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, Mexico

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ABSTRACT

Objective: To determine whether an association exists between the presence of rheumatoid nodules and thickening of the intima-media and plaque of the carotid artery, which is evidence of atherosclerosis.

Materials and methods: Observational, cross-sectional study of 124 patients with rheumatoid arthritis from a University Hospital clinic from 2005 to 2006. We divided the patients into 2 groups, 62 with rheumatoid nodules and 62 without rheumatoid nodules, matched for age and sex. Medical history, erythrocyte sedimentation rate, anti-cyclic citrullinated peptide, rheumatoid factor, and a high resolution doppler ultrasound of the carotid arteries were performed.

Results: Women comprised 89.5% of the patients. The prevalence of a carotid plaque was 57% in our population. The presence of a plaque was associated with age, arterial hypertension and abdominal circumference. Average intima-media thickness (IMT) in patients with a plaque was 0.085 cm ± 0.02. There was no correlation between laboratory parameters and thickening of the intima-media of the carotid artery. Subcutaneous nodules were present in 33 (47%) of the 70 patients with a carotid plaque and in 29 (54%) of patients without a carotid plaque (p = 0.471).

Conclusions: We did not find an association between rheumatoid nodules and the presence of a carotid plaque and thickening of the intima-media of the carotid in patients with rheumatoid arthritis.

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Atherosclerosis carotídica en pacientes con artritis reumatoide y nódulos reumatóides

RESUMEN

Objetivo: Determinar si existe una asociación entre la presencia de nódulos reumatóides y el engrosamiento de la íntima-media y de placa de las arterias carótidas.

Materiales y métodos: Estudio observacional, transversal de 124 pacientes con artritis reumatoide del Servicio de Reumatología de un Hospital Universitario desde 2005 a 2006. Se dividieron los pacientes en 2 grupos, 62 con nódulos reumatóides y 62 sin nódulos reumatóides, pareados por edad y sexo. Se realizó una historia clínica completa, velocidad de sedimentación globular, medición de anticuerpos antíptéptidos cíclicos citrullinados, factor reumatoide y una ecografía doppler de alta resolución de las arterias carótidas.

Resultados: Las mujeres comprendieron el 89.5% de los pacientes. La prevalencia de al menos una placa en las carótidas fue del 57% en nuestra población. La presencia de placa carotídea estuvo asociada a la edad, hipertensión arterial y circunferencia abdominal. El grosor promedio de la íntima-media en pacientes con placa carotídea fue 0.085 cm ± 0.02. No hubo ninguna correlación entre los parámetros de laboratorio y el engrosamiento de íntima-media de la arteria carótida. Los nódulos subcutáneos estuvieron presentes en 33 (47%) de los 70 pacientes con placas de carótida y 29 (54%) de los pacientes sin una placa carótida (p = 0.471).

* Corresponding author.
E-mail addresses: dgalarza@medicinauanl.mx, medint@hospitaluniversitario.org (D.A. Galarza-Delgado).

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Introduction

Rheumatoid arthritis (RA) is a chronic, inflammatory, multiscy-
temic, multifactorial, autoimmune disorder of unknown etiology
that affects mostly diarthrodial joints. RA has a prevalence of
1–2% in the general adult population. The greatest incidence occurs
between 35 and 45 years of age with predominance in women
of 3–1. It presents as a chronic, bilateral, symmetrical erosive
polyarthritis with diverse extrarticular manifestations that affect
issues and organs such as peripheral nerves, blood vessels, the
lung, eyes, heart, and spleen with the presence of rheumatoid nod-
ules, anemia, and symptoms of systemic disease. Three types of
clinical course are recognized in this disease: type I, a self-limited
process; type II, a polycyclic variant; and type III, the most frequent,
which is progressive and deforming. 2

Since the 1980s, RA has been known to lower life expectancy, 3–8
with a mortality rate similar to that observed in patients with
Hodgkin disease, diabetes mellitus, or cerebrovascular disease. 4
Life expectancy can decrease 4–7 years in men and 3–10 years in
women, but a decrease of up to 18 years has been reported. 9 The
mortality rate in patients with RA increases during the course of
the disease with a tendency to accelerate after 15 years. 10

The main causes of death are cardiovascular (37.4%), cerebrovas-
cular (9.4%), and pulmonary diseases (10%), neoplasias (10.3%),
and infections (15.2%). 6,9,11–21 This information is from hospital 22–28
and community studies 20,21 that confirm that mortality is due
mainly to cardiovascular disease. The incidence of cardiovascular
disease in RA patients is independent of traditional cardiovascu-
lar risk factors. 3,29–32 The underlying mechanism for this increase
has not been elucidated. Cardiovascular mortality has been cor-
related with greater activity of the disease (increased erythrocyte
sedimentation rate, 33 severe extra-articular manifestations, 34,35
rheumatoid factor seropositivity, 36 C-reactive protein, 36–38 and
the presence of rheumatoid nodules). The inflammation that occurs
in persons with RA has been suggested to accelerate the atheroscle-
rotic process. 30,36

Intima-media thickness of the wall of the common carotid artery
measured by high resolution ultrasound is a safe, non-invasive,
reproducible, clinically useful biomarker of early stage atheroscle-
rosis that correlates with coronary involvement. 39 This measure
has greater predictive power than cardiovascular risk factors. 40
Intima-media thickness in RA patients correlates with the duration
and severity of the disease. 33,36,41

The association between carotid atherosclerosis, confirmed by
ultrasound, and inflammatory markers, such as erythrocyte sedi-
mentation rate and C-reactive protein, is independent of age, sex,
and cardiovascular risk factors such as hypercholesterolemia, sys-
tolic arterial hypertension, 42 diabetes mellitus, 43,44 and body mass
index. 44

In RA, rheumatoid nodules are considered a manifestation of
more aggressive disease; patients with rheumatoid vasculitis are
known to have twice the probability of developing rheumatoid
nodules. 45,46 Therefore, we considered it important to evaluate
the correlation between atherosclerotic carotid disease and the
presence of a specific extra-articular manifestation of RA, nodules.
Rheumatoid nodules are tissue tumors that are usually located sub-
cutaneously and that can be found in diverse organs, including the
eye, lung, heart and brain. They are present in 20–40% of patients
with rheumatoid arthritis and are more frequent on extensor sur-
faces of the limbs such as the olecranon. Nodules vary in consistency
from a soft, amorphous, completely mobile mass to a hard mass
firmly attached to the periosteum. They differ in size from a few
millimeters to several centimeters and are usually painless. Their
histologic appearance is considered characteristic, although not
completely pathognomonic. Development of nodules is mediated
through effects on small arterioles and the resultant activation of
complement and terminal vasculitis.

In addition, another interesting point is the effect of anti-tumor
necrosis factor alpha therapy and the methotrexate on the progres-
sion of atherosclerosis in RA patients through the determination
of carotid IMT by ultrasound. In fact, several studies have shown
a reduction of carotid IMT in patients with active RA receiving this
medication. 47,48 Therefore, this image method could be a very use-
ful tool for regular assessment, monitoring and management of
cardiovascular risk in this population.

Patients and methods

The participants were patients who met at least 4 American Col-
lege of Rheumatology criteria for RA and who also attended the
Rheumatology Service of the Hospital Universitario “Dr. Jose Eleu-
terio Gonzalez” of the Universidad Autónoma of Nuevo León from
August 2005 to July 2006. The selection of patients with rheumatoid
nodules was not based on a consecutive sequence of attendance to
the clinic, but on an intentional search for the presence of nodules.
Patients with nodules were matched with RA patients that did not
have rheumatoid nodules according to age and sex.

Enrolled patients were greater than 16 years of age and provided
informed consent for participation. Pregnant patients or those with
a history of carotid surgery were excluded.

Clinical evaluation included a complete medical history with
determination of active rheumatoid arthritis inflammation using
the criteria previously mentioned 50; we also documented the pres-
ence of extra-articular manifestations. In order to find out a possible
association between IMT and antirheumatic therapy, including
methotrexate, biologic therapy (anti-TNF blockers), antimalarias,
and steroids, we classified the time of exposition to antirheumatic
drugs in categorical variable (0 = none, 1 = 1–6 months, 2 = 7–12
months, 3 = 1–3 years, 4 = 3–5 years, 5 = 5–7 years, 6 = 7–10 years,
7 = >10 years).

Patients filled out a validated self-applied questionnaire in
Spanish, the Modified Health Assessment Questionnaire (MHAQ). 27
The following laboratory tests were performed: complete blood
count, liver function tests, urinalysis, blood chemistry, and lipid
profile. Also, C-reactive protein, erythrocyte sedimentation rate,
rheumatoid factor, and anti-cyclic citrullinated peptide (anti-CCP)
antibody titer were measured.

To measure C-reactive protein, we used the Lafon Protex-CR
(Laboratorios Lafon, S.A. de C.V., Mexico) latex agglutination tech-
nique, which determines and quantifies C-reactive protein in serum
by an indirect method. 51 A test was positive when macroscopic
agglutination, and a clear plate bottom comparable to a positive
control at a dilution of 1:40, equivalent to a sensitivity of 1.0 mg/dL,
occurred.

Erythro sedimentation rate (ESR) was determined using the
Winthrope method. The upper limit of normal adjusted for age was
considered a significant result: for men it was obtained by dividing
the patient’s age by two, and in women, age plus ten divided by
two. 51
The Lafor Reumatex kit, in which the globulin latex reagent (polystyrene particles sensitized with human gamma-globulin) agglutinates in the presence of serum with the rheumatoid factor adequately diluted, was used to measure rheumatoid factor. A test was positive when macroscopic agglutination occurred with the formation of clumps at a dilution of 1:20.

The Axis-Shield Diastat (Axis Shield Diagnostics Ltd., UK) was used to determine anti-cyclic citrullinated peptide antibodies. This is a semiquantitative/qualitative enzyme-linked immunosorbent serologic assay (ELISA) for detecting specific IgG antibodies in human serum or plasma. The reference range considered positive was >5 U/ml.

The measurement of IMT was performed with the patient in supine position with a high-resolution ultrasonography (General Electric Logic 9) of both common carotid artery below its bifurcation and of the proximal internal carotid artery with a 14 MHz linear transducer. The arterial wall segments were assessed in a longitudinal view. The measurement of the IMT was performed bilaterally on the far wall of the common carotid artery taking into account for the analysis the thickest. Plaque thickness was expressed in centimeters. Measurements of intima-media thickness were obtained according to a standardized protocol. One radiologist performed all studies without clinical information about the patients.

Carotid intima-media thickness was evaluated according to the Mannheim Carotid Intima-Media Thickness Consensus (2004–2006), in which a plaque is defined as the focal structure that invades the lumen of the artery by at least 0.5 mm or 50% of the value of intima-media thickness, or when thickness is equal to or greater than 1.5 mm when measured from the adventitia-media interface to the intima-arterial lumen interface.

Statistical analysis

The number of patients needed for study was 124, with a $\beta$ value of 0.2 and an $\alpha$ value of 0.05, so the group was divided into 62 with rheumatoid nodules ($n$) and 62 without nodules.

We used a comparative univariate analysis with Student’s t-test for normally distributed variables, $\chi^2$ and Fisher’s exact test for non-normally distributed and binary variables, and Mann–Whitney and Kruskal–Wallis U-tests for non-parametric variables. We also did multivariate analysis with linear regression coefficient with variables that had $p<0.2$ and those were age, sex, hypertension, systolic blood pressure, waistline, thickness of the intima-media (TIM), hypercholesterolemia. Regarding the association between time of exposition of antirheumatic therapy and IMT we used a Spearman’s rank correlation coefficient.

Statistical significance was defined at $p<0.05$ for univariate and multivariate analysis.

The study protocol was evaluated and approved by the Research and Ethics Committee of the Facultad de Medicina and Hospital Universitario “Dr. Jose Eleuterio Gonzalez” of the Universidad Autonoma de Nuevo Leon (Registration no. RE-05-011). The study was financed by the Programa de Apoyo a Investigacion Cientifica y Tecnologica (PAICYT 2006) of the Universidad Autonoma de Nuevo Leon, code number SA1191-05.

Results

Of the 124 patients examined in this study, 111 were women (89.5%) and 13 were men (10.5%), with an average age of 55.5 years ($\pm13.1$).

The average duration of RA in the study population was 12.4 years ($\pm9.7$). Rheumatoid factor was positive in 92 patients (74%); 90 were anti-CCP positive (72%).

Fifty-five patients (44%) had hand deformities, 44 (35%) active disease and 80 (65%) were in remission. There was no difference between the groups regarding the use of different antirheumatic drugs including time of exposition (Table 1).

For the whole group, carotid intima-media thickening had a range of 0.04–0.17 cm, with an average of 0.08 cm ($\pm0.02$). The presence of an atherosclerotic plaque in the population was 57%. There were 70/124 (56.45%) patients with a carotid plaque with an average age of 62 years, while the average age of the 54 patients without a carotid plaque was 47 years ($p=0.001$). Of the patients with a plaque, 62 (89%) were women, while 49 (91%) were women without a plaque ($p=NS$).

In the age group of 30–39 years, no carotid plaque was found; in the group 40–49 years of age, it was detected in 25%; 50–59 years, 69.7%; 60–69 years, 80%; and in patients greater than 70 years, 84.2% (Fig. 1).

The average duration of disease in patients with a carotid plaque was 13.4 years ($\pm10.7$) while in those without a carotid plaque was 11 years ($\pm8.2$). In 33 (47%) of the 70 patients with a carotid plaque, the presence of subcutaneous nodules was found and in patients without a carotid plaque the nodules were found in 29 (54%) ($p=0.471$). There was no association between thickening of the intima-media or plaque and the clinical variables of rheumatoid arthritis, such as disease duration, joint deformity, morning stiffness, number of painful joints, number of inflamed joints, or rheumatoid nodules.

There was also no association between erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, anti-CCP antibodies, and the patients with or without a carotid plaque.

Among the traditional cardiovascular risk factors, only hypertension, as well as waistline circumference, showed an association with the presence of a carotid plaque.

Average intima-media thickness in patients with a plaque was 0.086 cm ($\pm0.02$).

One-third of the studied population had an average age of 64.8 years ($\pm9.3$) ($p<0.001$) and this correlated with the presence of thickening of the carotid intima-media ($p=0.001$).

We were not able to find an association between the time of exposition to the antirheumatic drugs and IMT or carotid plaque; however, the correlation analysis showed a trend for the time of exposition to methotrexate ($p=0.064$) and the use of anti-TNF ($p=0.079$) and a lower IMT at the common carotid artery.

Discussion

Contrary to our hypothesis, in our population of 124 patients with RA, there was no association between the presence of rheumatoid nodules and ultrasonographic evidence of carotid atherosclerosis (intima-media thickness and plaque).
Table 1
Characteristics of patients with rheumatoid arthritis.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whole RA group</th>
<th>RA patients w/o nodules</th>
<th>RA patients with nodules</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>124</td>
<td>62</td>
<td>62</td>
<td>NS</td>
</tr>
<tr>
<td>Men (n)</td>
<td>13</td>
<td>7</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Women (n)</td>
<td>111</td>
<td>55</td>
<td>56</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>55.5 (10.8)</td>
<td>56.97 (12.65)</td>
<td>54.03 (13.45)</td>
<td>NS</td>
</tr>
<tr>
<td>Time of evolution of RA, mean (SD)</td>
<td>12.38 (9.71)</td>
<td>10.94 (9.37)</td>
<td>13.84 (9.92)</td>
<td>NS</td>
</tr>
<tr>
<td>Hand deformities, n (%)</td>
<td>54 (44)</td>
<td>17 (27.4)</td>
<td>37 (59.7)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Active disease, n (%)</td>
<td>44 (35)</td>
<td>15 (24.2)</td>
<td>29 (46.8)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Disease in remission, n (%)</td>
<td>80 (65)</td>
<td>47 (75.8)</td>
<td>33 (53.2)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Positive rheumatoid factor, n (%)</td>
<td>92 (74)</td>
<td>39 (62.9)</td>
<td>53 (85.5)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Positive anti-CCP, n (%)</td>
<td>90 (72)</td>
<td>35 (56.5)</td>
<td>55 (88.7)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>58 (71%)</td>
<td>46 (74%)</td>
<td>42 (68%)</td>
<td>0.429</td>
</tr>
<tr>
<td>TE (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.507</td>
</tr>
<tr>
<td>Antimalarial drugs</td>
<td>51 (41%)</td>
<td>28 (45%)</td>
<td>23 (37%)</td>
<td>0.362</td>
</tr>
<tr>
<td>TE (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.283</td>
</tr>
<tr>
<td>Biological therapy</td>
<td>27 (21.7%)</td>
<td>14 (23%)</td>
<td>13 (21%)</td>
<td>0.828</td>
</tr>
<tr>
<td>TE (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.688</td>
</tr>
<tr>
<td>Steroids</td>
<td>68 (55%)</td>
<td>39 (63%)</td>
<td>29 (47%)</td>
<td>0.071</td>
</tr>
<tr>
<td>TE (%)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0.075</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>36 (29)</td>
<td>21 (33.9)</td>
<td>15 (24.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>19 (15)</td>
<td>13 (21)</td>
<td>6 (9.7)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²), mean (DS)</td>
<td>27.8 (4.8)</td>
<td>28.49 (5.26)</td>
<td>27.1 (4.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Waistline circumference (cm), mean (DS)</td>
<td>88.4 (14.3)</td>
<td>90.58 (15.5)</td>
<td>86.21 (12.73)</td>
<td>NS</td>
</tr>
<tr>
<td>Tobacco use, n (%)</td>
<td>40 (39.5)</td>
<td>28 (45.16)</td>
<td>21 (33.9)</td>
<td>NS</td>
</tr>
<tr>
<td>IMT (cm), mean (DS)</td>
<td>0.07654 (0.020)</td>
<td>0.076 (0.019)</td>
<td>0.077 (0.022)</td>
<td>NS</td>
</tr>
<tr>
<td>Patients with a plaque, n (%)</td>
<td>70 (57)</td>
<td>37 (59.7)</td>
<td>33 (53.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

a Chi square test.
b IMT: intima-media thickness.
c TE: time of exposition measure as categorical variable, 0 = none, 1 = 1–6 months, 2 = 7–12 months, 3 = 1–3 years, 4 = 3–5 years, 5 = 5–7 years, 6 = 7–10 years, 7 = >10 years.

On the other hand, it was notable in this study that the prevalence of carotid plaque in our population was 57%, which is greater than the 44% found by Roman53 in New York, in an Anglo-Saxon patient population with rheumatoid arthritis, and higher than the 15% found in control subjects without rheumatoid arthritis in the same population.

As was expected, age, a known cardiovascular risk factor, was the variable that was most associated with the presence of a carotid plaque and to thickening of the intima-media. The data of this population is comparable with world statistics, which indicate that an increase in the prevalence of carotid plaque is directly proportional to the age of the individuals.

Besides age, two other factors that correlated with the presence of a plaque were hypertension and waistline circumference, which are also factors described for cardiovascular disease (Table 2).

With regard to clinical manifestations of rheumatoid arthritis, we did not find any parameter associated with a greater prevalence of plaque or intima-media thickness, although it is worthy to point out that duration of the disease tended to be greater in the upper third with regard to intima-media thickness.

Table 2
Cardiovascular risk factors found in the univariate analysis of independent variables vs. the presence of carotid plaque.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Carotid plaque present, n = 70</th>
<th>Carotid plaque absent, n = 54</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>9 (13)</td>
<td>7 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>28 (40)</td>
<td>8 (15)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>128.5 (SD 16.7)</td>
<td>120.2 (SD 12.5)</td>
<td>0.011</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80.4 (SD 9.4)</td>
<td>77.6 (SD 7.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>29 (41)</td>
<td>19 (35)</td>
<td>NS</td>
</tr>
<tr>
<td>Tobacco use, n (%)</td>
<td>28 (40)</td>
<td>21 (39)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.9 (SD 4.8)</td>
<td>27.7 (SD 4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Waistline circumference (cm)</td>
<td>90.7 (SD 13)</td>
<td>85.2 (SD 15.5)</td>
<td>0.017*</td>
</tr>
<tr>
<td>IMT (cm)</td>
<td>0.08564 (SD 0.02041)</td>
<td>0.06453 (SD 0.01278)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

a Body mass index.
b Intima-media thickness.
c Student’s t.
diabetes mellitus, have a greater incidence in Mexican population with regard to non-Hispanic whites.\textsuperscript{54}

Other potential factors that can contribute to this difference could be related to educational and sociocultural aspects, which would have as a consequence poor compliance to treatment, and therefore, poor control of the inflammatory activity of RA in our population, as well as a lower use in our setting of biological agents (undemonstrated data); drugs that not only show an important ability to induce remission in rheumatoid arthritis, but that also decrease cardiovascular complications in patients with RA.\textsuperscript{55-57}

Recently, the presence of anti-CCP antibodies and RF IgM has been associated with endothelial dysfunction in patients with rheumatoid arthritis independent of other cardiovascular risk factors in RA patients, but it was not evaluated in our work.\textsuperscript{58}

Currently, there is a consensus about the extreme usefulness of the carotid ultrasound in detecting subclinical atherosclerotic findings in patients with long-term RA without clinically evident atherosclerotic disease, as showed by Gonzalez-Juanatey et al.\textsuperscript{59}

They were able to demonstrate greater carotid IMT in a population of 47 patients comparing with controls, and the relationship between carotid plaques and a longer disease duration and more extraarticular manifestations. Age at the time of study and disease duration were the best predictive factors for the development of atherosclerotic disease.\textsuperscript{59}

Of paramount importance is the potential utility of carotid ultrasound in the prognosis value of subclinical atherosclerosis in RA and its application in monitoring the effect of new biological drugs in the evolution of atherosclerotic disease.\textsuperscript{48} Carotid IMT has been used as a marker of progression of atherosclerosis in RA patients undergoing treatment with anti-tumor necrosis factor alpha blockers due to severe disease, and refractory to methotrexate.\textsuperscript{49} In a study response to anti-tumor necrosis factor alpha blockade was associated with reduction of carotid intima-media thickness in patients with active rheumatoid arthritis.\textsuperscript{58}

In our study, however, we did not find an effect of the use of methotrexate, anti-TNF blockers, antimalarials or steroids, on the IMT, even though there was a trend to lower IMT with the first two of them.

Interestingly, an association between the magnitude and chronicity of the inflammatory response, determined as the mean C-reactive protein in long-standing RA patients without clinically evident cardiovascular disease and the carotid IMT values has also been reported.\textsuperscript{50}

Conclusions

We did not find an association between the presence of rheumatoid nodules and thickening of the intima-media, and plaque of the carotid artery as evidence of atherosclerosis in patients with rheumatoid arthritis.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. The study protocol was evaluated and approved by the Research and Ethics Committee of the Facultad de Medicina and Hospital Universitario “Dr. Jose Eleuterio Gonzalez” of the Universidad Autonoma de Nuevo Leon (Registration no. RE-05-011). Enrolled patients were older than 18 years of age and provided informed consent for participation. Pregnant patients or those with a history of carotid surgery were excluded.

Funding

The study was financed by the Programa de Apoyo a Investigacion Cientifica y Tecnologica (PAICYT) 2006 of the Universidad Autonoma de Nuevo Leon, code number SA1191-05. Clinical evaluation included a complete medical history, self-applied questionnaire in Spanish, routine lab tests, and Bilateral high-resolution ultrasonography was performed of the common carotid artery.

Conflict of interest

No conflict of interest.

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References


