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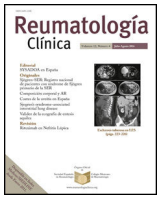

Brief Report

Cardiovascular event in a cohort of rheumatoid arthritis patients in Castilla-La Mancha: Utility of carotid ultrasound

Marco Aurelio Ramírez Huaranga,[a,*] David Velasco Sánchez,[a] Luis Ángel Calvo Pascual,[b] David Castro Corredor,[a] María Dolores Mínguez Sánchez,[a] Verónica Salas Manzanedo,[a] Eva Revuelta Evrard,[a] Rocío Arenal López,[a] Joaquín Anino Fernández,[a] Marina González Peñas,[a] Lourdes Martin de la Sierra López,[a] Laura María Jiménez Rodríguez,[a] Alberto López Menchero Mora,[a] Marcos Paulino Huertas[a]

[a] *Servicio de Reumatología, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain*
[b] *Departamento de Métodos Cuantitativos, ICADE, Universidad Pontificia de Comillas, Madrid, Spain*

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ABSTRACT

Rheumatoid Arthritis (RA) has a mortality rate 1,3 to 3 times higher than the general population, with cardiovascular mortality accounting for 40–50% of cases. Currently, cardiovascular disease is considered an extraarticular manifestation of RA (OR: 1,5–4,0). Ultrasound measurement of the intima-media thickness (IMT) of the common carotid artery and the presence of atherosclerotic plaques (AP) is a non-invasive method and a surrogate marker of subclinical arteriosclerosis.

Objective: To determine if subclinical arteriosclerosis findings through carotid ultrasound can serve as a good predictor of cardiovascular events (CVE) development in a cohort of RA patients over a 10-year period.

Methodology: A cohort of RA patients seen in the Rheumatology outpatient clinic of a hospital in Castilla La Mancha in 2013 was evaluated. A prospective evaluation for the development of CVE over the following 10 years was conducted, and its correlation with previous ultrasound findings of IMT and AP was analyzed.

Results: Eight (24%) patients experienced a CVE. Three (9%) had heart failure, three (9%) had a stroke, and two (6%) experienced acute myocardial infarction. RA patients who developed a CVE had a higher IMT (0,97 +/− 0.08 mm) compared to the RA patients without CV complications (0,74 +/− 0.15 mm) ($p = 0{,}003$). The presence of IMT $\geq$ 0.9 mm and AP had a relative risk of 12,25 ($p = 0{,}012$) and 18,66 ($p = 0{,}003$), respectively, for the development of a CVE.

Conclusions: Carotid ultrasound in RA patients may allow for early detection of subclinical atherosclerosis before the development of CVE, with IMT $\geq$ 0.9 mm being the most closely associated finding with CVE, unaffected by age.

Evento cardiovascular en una cohorte de pacientes con artritis reumatoide en Castilla-La Mancha, utilidad de la ecografía carotídea

Palabras clave:
Artritis reumatoide
Ecografía carotídea
Placa ateromatosa
Grosor íntimo medial
Evento cardiovascular

RESUMEN

La Artritis Reumatoide (AR) presenta una mortalidad de 1,3 a 3 veces superior a la población general donde destaca la mortalidad de origen cardiovascular con un 40–50%. Actualmente se considera a la enfermedad cardiovascular como una manifestación extraarticular de la AR, siendo un factor de riesgo independiente de los tradicionales, con un riesgo elevado de enfermedad cardiovascular (OR: 1,5–4,0). La medición ecográfica del grosor íntimo medial (GIM) de la arteria carótida común y la presencia de placas ateromatosas (PA) es un método no invasivo y marcador subrogado de arterioesclerosis subclínica.

* Corresponding author.
E-mail address: maramirezh@sescam.jccm.es (M.A. Ramírez Huaranga).

Objetivo: Establecer si los hallazgos de arterioesclerosis subclínica por ecografía carotídea pueden ser un buen predictor del desarrollo de eventos cardiovasculares (ECV) en una cohorte de pacientes con AR a 10 años.
Metodología: Se evaluó una cohorte de pacientes con AR atendidos en consulta externa de Reumatología de una hospital de Castilla La Mancha durante el año 2013. Se realizó una evaluación para el desarrollo de ECV a los 10 años siguientes de comenzado el estudio y se analizó su correlación con los hallazgos ecográficos previos de GIM y PA.
Resultados: 8 (24%) pacientes presentaron un ECV. 3 (9%) episodio de Fallo cardiaco, 3 (9%) accidente cerebro vascular y 2 (6%) episodio de infarto agudo al miocardio. Los pacientes con AR que desarrollaron un ECV habían presentado un GIM mayor (0,97 +/− 0,08 mm) en comparación con los pacientes con AR que no tuvieron complicaciones CV (0,74 +/− 0,15 mm) (p = 0,003). La presencia de un a GIM ≥ 0,9 mm y PA presentó un riesgo relativo de 12,25 (p = 0,012) y 18,66 (p = 0,003), respectivamente, para el desarrollo de un ECV.
Conclusiones: La ecografía carotídea en pacientes con AR nos podría permitir la detección precoz de aterosclerosis subclínica antes del desarrollo de ECV, siendo fundamentalmente el GIM ≥ 0,9 mm el hallazgo más asociado a ECV y no influenciado por la edad.

Introduction

It has been known for many years that the state of chronic inflammation, regardless of its origin and translated into the presence of markers of inflammation, is considered a predictor of cardiovascular events (CVEs).[1] Rheumatoid arthritis (RA), the prototype of chronic systemic inflammatory diseases, affects 0.5–1% of the population and has a mortality rate that is 1.3–3 times higher than in the general population, with cardiovascular mortality standing out at 40–50%.[2] For several years, an increased risk of heart attack (relative risk [RR]: 2.0–2.13) and stroke (RR: 1.48–1.94)[3,4] has been evidenced in this group of patients, with cardiovascular disease currently being considered an extra-articular manifestation of RA. This is a risk factor which is independent of traditional ones, demonstrating a high risk of cardiovascular disease (OR: 1.5–4.0).[5–8] This explains why, more than a decade ago, the European League Against Rheumatic Diseases (EULAR) proposed the modified SCORE (mSCORE) for the assessment of cardiovascular risk (CVR). This consisted of multiplying the result obtained with SCORE by a conversion factor of 1.5 for patients who met 2 of the following 3 criteria:[9]

- Duration of disease ≥ 10 years.
- Rheumatoid factor and/or positive cyclic citrullinated antipeptide.
- The presence of extra-articular manifestations.

However, over the years, it has been observed that this tool underestimates this risk. In groups classified as low and intermediate risk, the presence of subclinical atherosclerosis and the development of short- to medium-term CVEs was observed by carotid ultrasound in up to 12–30% of cases.[10–12]

This led to the search for additional tools to help identify the level of CVR more accurately. Of these, the use of carotid ultrasound has now gained great relevance and clinical usefulness,[13–15] considering the measurement of the intima-media thickness (IMT) of the common carotid artery and the presence of atheromatous plaques (APs), which is a non-invasive method and surrogate marker of subclinical arteriosclerosis.

Our team conducted a study 10 years ago on a cohort of patients with RA that confirmed the lack of correlation between the mSCORE and the findings of subclinical arteriosclerosis by carotid ultrasound, as well as the increase in CVR due to IMT ≥ 0.9 mm and the presence of BP in patients with RA, fundamentally associated with the degree of systemic activity.[16,17]

The aim of the present study was to establish whether findings of subclinical arteriosclerosis by carotid ultrasound may be a good predictor of the development of CVEs in a 10-year cohort of RA patients.

Methodology

A cohort of patients with RA, treated at the Rheumatology outpatient clinic of a hospital in Castilla-La Mancha during 2013, was evaluated. The study was approved by the local institutional ethics committee and informed consent was obtained from all patients. Information on the clinical profile, factors, and stratification of CVR has been published previously.[16,17] The initial cohort consisted of 119 patients (63.8% female) with a mean age of 57.43 ± 13.63 years, an average body mass index of 27.44 ± 5.04 kg/m^2, and with the following clinical profile: 25 (21%) smokers; 48 (40.3%) with hypertension; 36 (30%) with dyslipidaemia, 4 (3.36%) with diabetes mellitus; 2 (1.68%) with renal failure 8 (6.72%) had previous CVEs; 56 (47%) had more than 10 years of disease progression; 58 (48.7%) had rheumatoid factor (+); 82 (68.9%) had cyclic citrullinated peptide (+); and 28 (23.53%) had extra-articular manifestations. The same vascular radiologist, who was also unaware at all times of the risk group of each patient, performed the carotid ultrasound following his usual examination protocol with the same Toshiba Aplio XG ultrasound machine, model Ssa-790A, 7−10 MHz linear transducer. The presence of atheromatous plaque was shown in 31 (31.63%) patients (focal thickening > 1.5 mm in comparison with the adjacent IMT) and in 19 (19.39%) patients an IMT of ≥ 0.90 mm (average value obtained from the distance between the carotid-intimal lumen interface and the media-adventitious interface of the distal wall along 10 mm at 3 different points of each carotid artery), both of these being considered as data indicating subclinical atherosclerosis.

At 10 years after the initial evaluation of CVR factors, risk stratification, and carotid ultrasound in this cohort of patients, a review of the clinical history was run and all CVEs that had occurred over the 10-year period were recorded (no further risk stratification or carotid ultrasound control was run). For this part of the study, patients with a personal history of CVEs, hypertension, diabetes mellitus, dyslipidaemia, renal failure, obesity (body mass index ≥ 30 kg/m^2) and smokers were excluded in order to minimise risk factors that could influence the development of CVEs. Throughout the 10 years of the study, 2 patients discontinued follow-up in our hospital, thus the final group was composed of 33 patients. In addition to the clinical presentation, ischaemic heart disease was

confirmed by electrocardiogram and cardiac biomarkers; strokes by magnetic resonance imaging and/or brain CT scan; peripheral artery disease by Doppler/arteriography; and heart failure by chest x-ray and laboratory markers.

The information collected was included in a Microsoft Excel database designed for the study. Quantitative variables were presented as mean and standard deviation, and qualitative variables as a number and percentage. The Shapiro-Wilk test was run to evaluate the normality of the data for the primary endpoint (IMP) and since no significantly different distribution from a normal distribution was observed, the Student's t-test was used for these paired quantitative variables. To assess the association between the results of ultrasound findings and the development of CVEs, we calculated the RR.

To observe the behaviour of CVEs at 10 years, the previous classic statistics was supplemented with a box plot to visualise how the distribution, median, quartiles, and outliers of the IMP variable varied, depending on whether or not CVEs existed.

Subsequently, a selection was made of the most significant variables. It was considered that the best statistical analysis for this purpose was the mutual information test,[18] since it not only records direct or linear relationships between variables, such as the classic F or chi tests, but also captures complex and inverse relationships, etc. Once the most significant variables were selected, their ROC curves were examined, classifying being based on the values of the variable, depending on the presence of CVEs or not, A high area under the curve meant that the variable under study (IMT or BP) was sensitive to CVEs.

All analyses were run with a 95% confidence level using STATA 12.0.

Results

Within 10 years of the initial assessment of CVR using the mSCORE and carotid ultrasound, 8 (24%) patients presented a CVE, while 3 of them had a second subsequent episode. Three (9%) had episodes of heart failure, 3 (9%) strokes, and 2 (6%) had episodes of acute myocardial infarction. The first CVE was recorded 3 years after the start of the study and the most recent one at 9 years. For the purposes of the analysis, the patient was taken as the unit of measurement, not the event. Only one death was recorded, due to haemorrhagic shock in relation to peptic ulcer. The clinical features are presented in Table 1.

Patients with RA who developed a CVE had a higher IMT (0.97 ± 0.08 mm) compared to the rest of the RA patients who did not have any CVEs (0.74 ± 0.15 mm) ($p = 0.003$). Age was not a determining factor since there were no differences ($p = 1.19$) in age between patients with an IMT of $\geq 0,9$ mm (49.67 ± 9.86 years) and those with an IMT of < 0.9 mm (48.48 ± 11.75 years). In addition, 7 of the 9 patients with BP (77.8%) developed a CVE at 10 years. The presence of BP did have a significant association ($p = 0.0001$) with a higher mean age (60.22 ± 10.15 years) as compared to those who were negative for this finding (44.67 ± 7.89 years).

When analysing the association between IMT and the presence of BP as a predictor of the development of a CVE over the next 10 years, it was observed that the presence of an IMT ≥ 0.9 mm and atheromatous plaque presented an RR of 12.25 ($p = 0.012$; 95% CI: 1.70–87.98) and 18.66 ($p = 0.003$; 95% CI: 2.65–131.23), respectively, for the development of a CVE. The ROC curves (Fig. 1) confirm the sensitivity of IMT and BP variables to a CVE and show very high areas under the curve with values of 0.91 and 0.90, respectively.

After analysing the variables: time of evolution > 10 years ($p = 0.77$); presence of rheumatoid factor ($p = 0.21$) or ACPA ($p = 0.96$), no significant association was observed. However, as expected, age was a significant determinant ($p = 0.009$) for the development of a CVE (57.38 ± 10.47 years) compared to those who did not present this outcome (46.2 ± 9.82 years). The mutual information tests enabled us to identify the most significant variables in the occurrence of a CVE: mSCORE (0.35); BP = atheromatous plaque (0.33); activity = disease activity (0.26) and IMT = intima-media thickness (0.22).

Table 1
Clinical characteristics and cardiovascular risk assessment of our cohort of RA patients (n = 33).

Variables	N	% or SD
Gender: female	22	66.6
Mean age (years)	48.9	±10.95
Time from diagnosis to completion of the study (years)	19.5	±5.9
Rheumatoid factor (+)	18	54.5
Citrullinated cyclic antipeptides (+)	29	87.8
Cardiovascular risk according to mSCORE		
Very high risk	0	0
High risk	0	0
Intermediate risk	12	36.4
Low risk	11	33.3
Carotid ultrasound findings		
Mean value of intima-media thickness	079	±0.17
Intima-media thickness > 0 = 0.9 mm	12	36.4
Presence of atheromatous plaque	9	27.3
First cardiovascular event at 10 years		
Acute myocardial infarction	2	6
Stroke	3	9
Peripheral artery disease	0	0
Heart failure	3	9
Second cardiovascular event at 10 years		
Acute myocardial infarction	1	3
Stroke	2	6
Peripheral artery disease	0	0
Heart failure	0	0

Discussion

The results of our study show that the findings of subclinical arteriosclerosis by carotid ultrasound have a high predictive value for the development of CVEs at 10 years in our patients with RA, without other CVR factors being known at the time of the ultrasound study. IMT ≥ 0.9 mm was the determining factor, not significantly influenced by age.

More than a decade ago, Gonzalez-Juanatey et al. conducted a 5-year prospective study in a series of patients with RA, finding that 17% had CVEs at 5 years of follow-up (9% myocardial infarction, 6% stroke, and 2% peripheral artery disease) and 6% died from a CVE.[19] Another study observed that at 5 years of follow-up a cohort of patients with RA presented an increase in CVEs (3.9% stroke; 1.6% heart failure and 3.1% myocardial infarction) that was significantly higher than in a healthy population with similar clinical characteristics and comorbidities, concluding that patients with RA have a 5-year CVE risk of 1.33 (95% CI: 1,07−1,65; $p = 0.010$).[20] Finally, a recent study conducted by Corrales et al. on 327 patients with RA, without any other CVR factors, observed that 8.25% had a CVE over the next 5 years,[21] while in our 10-year cohort 24% had a CVE (9% heart failure, 9% stroke, and 6% acute myocardial infarction).

With respect to carotid ultrasound, Gonzalez-Juanatey et al. observed a higher carotid IMT in patients with RA who experienced a CVE during follow-up (1.01 ± 0.16 mm) compared to the remaining RA patients who did not have CV complications (0.74 ± 0.12 mm) ($p = 0.001$), concluding that carotid IMT could have high predictive power for the development of a CVE during the 5-year follow-up period. Therefore, these authors proposed doing a carotid ultrasound on all patients with RA to establish a subgroup of patients at high risk of CV[19] complications. On the other hand, another study conducted on 138 patients with RA that assessed the predictive value of IMT, or the presence of BP, determined that at

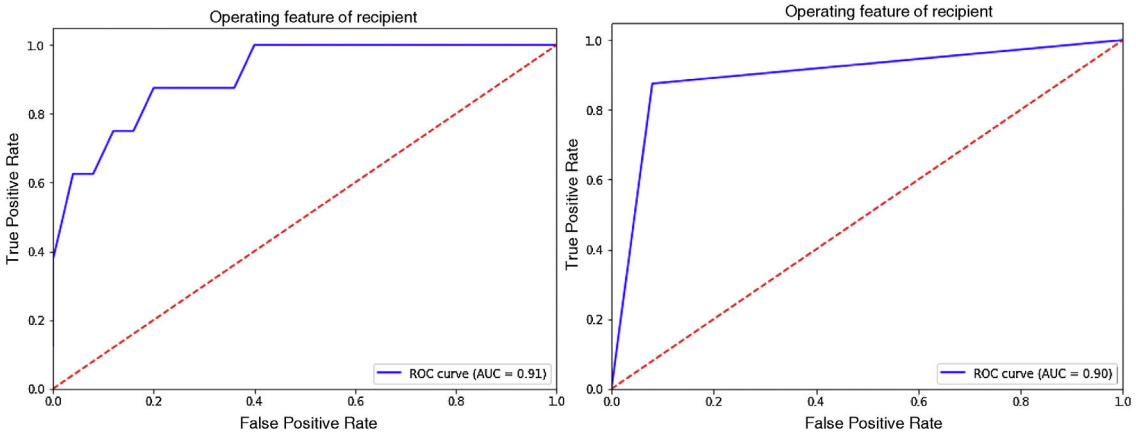

Figure 1. ROC curves where the target variable is risk of cardiovascular and the classification variable is IMT in the first case and BP in the second.

5.8 ± 0.8 years, 10 patients had experienced a total of 11 (7.97%) CVEs. In addition to age (p = 0.01) and chronic corticosteroid therapy (p = 0.01), elevated IMT (≥ 0.9 mm) was associated with the development of CVEs (p = 0.01) with a risk of 1.65 (95% CI: 1.27.2,13; p < 0.001) for each 0.1 mm increase in IMT.[22] In our cohort of RA patients, the development of CVEs was associated with a higher IMT (0.97 ± 0.08 mm) compared to the rest of the RA patients who did not have CV complications (0.74 ± 0.15 mm) (p = 0.003), while age was not a determining factor (p = 1.19). This gives an IMT ≥ 0, 9 mm RR of 12.25 (p = 0.012; 95% CI: 1.70–87.98) and BP an RR of 18.66 (p = 0.003; 95% CI: 2.65–131.23). The risk associated with the presence of BP was higher than that observed in other studies that presented a risk of 5.25 (95% CI: 1.41–19.50; p = 0.01) for these CVEs.[21]

Currently, more than 2000 articles have been published showing how carotid IMT and the presence of BP are currently good predictors of CVR.[23] However, age is a factor that is directly associated with an increase in IMT, with normal parameters in men considered to be between 0.59 mm in those under 25 years of age and 0.95 mm in those over 65 years of age. In women, the upper limit of normal ranged from 0.52 mm in those under 25 years of age to 0.93 mm in those over 65 years of age.[24] Carotid ultrasound continues to be the ideal imaging technique to improve CVE risk assessment in RA patients because most CVR calculators that have been developed underestimate the risk of CVEs.[25]

Given the high prevalence of cardiovascular disease in the RA population,[4,7] where it has been shown that systemic inflammatory disease activity is associated with higher CVR, the involvement of the rheumatologist in the assessment of this risk is vitally important.

This risk is also underlined by the pathological findings on carotid ultrasound, CVEs,[7,16] and the remission status or low inflammatory activity that is associated with the control of traditional CVR factors which correlates with the reduction of CVR in this group of patients.[5,6,9]

Currently, the use of ultrasound is common in the clinical practice of most rheumatology services and carotid ultrasound is a technique that has been incorporated into our portfolio of services such as capillaroscopy and biopsies, etc. Therefore, performing this procedure as a low-cost, non-invasive, dynamic and fast-performing tool will enable us to correctly stratify CVR in our patients.[13,26,27]

Conclusions

Carotid ultrasound in patients with RA could enable early detection of subclinical atherosclerosis before the development of CVEs, with IMT ≥ 0.9 mm being fundamentally the finding most associated with CVEs and not influenced by age. Therefore, we propose that an ultrasound evaluation of the carotid artery should be run on all patients with RA to establish a subgroup of patients at high risk of CVEs who will require better control of inflammatory disease and traditional risk factors.

Limitations

Although the sample size is small, the results of the study are similar to those obtained by other studies with larger numbers of patients. In addition, although patients with prior events and known traditional CVR factors were not included in the analysis, the lack of successive follow-ups over the 10 years following the initial study and the patient age may also have influenced the results.

Conflict of interest

None of the authors declare any conflicts of interest.

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References

1. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002;105:1135–43.
2. Toledano E, Candelas G, Rosales Z, Martínez-Prada C, León L, Abásolo L, et al. A meta-analysis of mortality in rheumatic diseases. Reumatol Clin. 2012;8:334–41.
3. Maradit-Kremers H, Crowson CS, Nicola PJ, Ballman KV, Roger VL, Jacobsen SJ, et al. Incresed unrecognized coronary heart disease and sudden deaths in rheumatoid arthritis: a population based cohort study. Arthritis Rheum. 2005;52:402–11.
4. Pieringer H, Pchiler M. Cardiovascular morbidity and mortality in patients with rheumatoid arthritis:vascular alterations and possible clinical implications. Q J Med. 2011;104:13–26.
5. Micha R, Imamura F, Wyler von Ballmoos M, Solomon DH, Hernán MA, Ridker PM, et al. Systematic review and meta-analysis of methotrexate use and risk of cardiovascular disease. Am J Cardiol. 2011;108:1362–70.
6. Provan SA, Semb AG, Hisdal J, Stranden E, Agewall S, Dagfinrud H, et al. Remission is the goal for cardiovascular risk managment in the patients with rheumatoid arthritis: a cross-sectional comparative study. Ann Rheum Dis. 2011;70:812–7.
7. Gkaliagkousi E, Gavriilaki E, Dounmas M, Petidis K, Aslanidis S, Stella D. Cardiovascular risk in rheumatoid arthritis: pathogenesis, diagnosis and management. J Clin Rheumatol. 2012;18:422–30.
8. Ráček V, Němec P. Rheumatoid arthritis - an independent risk factor for cardiovascular disease. Vnitr Lek. 2012;58:834–8.

9. Peters MJ, Symmons DP, McCarey D, Dijkmans BA, Nicola P, Kvien TK, et al. EULAR evidence-based recommendations for cardiovascular risk managment in patiens with rheumatoid arthritis and other forms of inflamatory arthritis. Ann Rheum Dis. 2010;69:325–31.
10. Gómez-Vaquero C, Robustillo M, Narváez J, Rodríguez-Moreno J, González-Juanatey C, Llorca J, et al. Assessment of cardiovascular risk in rheumatoid arthritis: impact of the new EULAR recommendations on the score cardiovascular risk index. Clin Rheumatol. 2012;31:35–9.
11. Rosales JL, Salvatierra J, Llorca J, Magro C, González MA, Cantero J, et al. Cardiovascular risk assessment in rheumatoid arthritis: impact of the EULAR recommendations on a national calibrated score risk index. Clin Exp Rheumatol. 2014;32:237–42.
12. Arts EEA, Popa C, Den Broeder AA, Semb AG, Toms T, Kitas GD, et al. Performance of four current risk algorithms in predicting cardiovascular events in patients with early rheumatoid arthritis. Ann Rheum Dis. 2015;74:668–74.
13. Corrales A, González-Juanatey C, Peiró ME, Blanco R, Llorca J, González-Gay MA. Carotid ultrasound is useful for the cardiovascular risk stratification of patients with rheumatoid arthritis: results of a population-based study. Ann Rheum Dis. 2014;73:722–7.
14. González-Gay MA, González-Juanatey C, Llorca J. Carotid ultrasound in the cardiovascular risk stratification of patients with rheumatoid arthritis: when and for whom? Ann Rheum Dis. 2012;71:796–8.
15. Corrales A, Parras JA, González-Juanatey C, Rueda-Gotor J, Blanco R, Llorca J, et al. Cardiovascular risk stratification in rheumatic diseases: carotid ultrasound is more sensitive than Coronary Artery Calcification Score to detect subclinical atherosclerosis in patients with rheumatoid arthritis. Ann Rheum Dis. 2013;72:1764–70.
16. Ramírez MA, Mínguez MD, Zarca MÁ, Espinoza PJ, Romero G. What role does rheumatoid arthritis disease activity have in cardiovascular risk. Reumatol Clin. 2018;14:339–45.
17. Ramirez MA, Minguez MD, Zarca MA, Ramos MI, Cuadra JL, Romero G. Artritis reumatoide, una enfermedad sistémica con un riesgo cardiovascular subestimado. Rev Colomb Reumatol. 2018;25:92–8.
18. Brown G, Pocock A, Zhao MJ, Luján M. Conditional likelihood maximisation: a unifying framework for information theoretic feature selection. J Mach Learn Res. 2006;7:1287–308.
19. Gonzalez-Juanatey C, Llorca J, Martin J, Gonzalez-Gay MA. Carotid intima-media thickness predicts the development of cardiovascular events in patients with rheumatoid arthritis. Semin Arthritis Rheum. 2009;38(5):366–71.
20. Nikiphorou E, De Lusignan S, Mallen CD, D Mallen C, Khavandi K, Bedarida G, et al. Heart. 2020;106:1566–72.
21. Corrales A, Vegas-Revenga N, Rueda-Gotor J, Portilla V, Atienza-Mateo B, Blanco R, et al. Carotid plaques as predictors of cardiovascular events in patients with Rheumatoid Arthritis. Results from a 5-year-prospective follow-up study. Semin Arthritis Rheum. 2020;50(6):1333–8.
22. Ikdahl E, Rollefstad S, Wibetoe G, Olsen IC, Berg IJ, Hisdal J, et al. Predictive Value of Arterial Stiffness and Subclinical Carotid Atherosclerosis for Cardiovascular Disease in Patients with Rheumatoid Arthritis. J Rheumatol. 2016;43(9):1622–30.
23. Saba L, Jamthikar A, Gupta D, Khanna NN, Viskovic K, Suri HS, et al. Global perspective on carotid intima-media thickness and plaque: should the current measurement guidelines be revisited? Int Angiol. 2019;38(6):451–65.
24. Jarauta E, Mateo-Gallego R, Bea A, Burillo E, Calmarza P, Civeira F. Carotid intima-media thickness in subjects with no cardiovascular risk factors. Rev Esp Cardiol. 2010;63(1):97–102.
25. Jamthikar AD, Gupta D, Puvvula A, Johri AM, Khanna NN, Saba L, et al. Cardiovascular risk assessment in patients with rheumatoid arthritis using carotid ultrasound B-mode imaging. Rheumatol Int. 2020;40(12):1921–39.
26. Semb AG, Rollefstad S, Van Riel P, Kitas G, Matteson E, Gabriel S. Cardiovascular disease assessment in rheumatoid arthritis: a guide to translating knowledge of cardiovascular risk into clinical practice. Ann Rheum Dis. 2014;73:1284–8.
27. Semb AG, Rollefstad S, Provan SA, Kvien TK, Stranden E, Olsen IC, et al. Carotid plaque characteristics and disease activity in rheumatoid arthritis. J Rheumatol. 2013;40:359–68.