Published in final edited form as:

Clin Rheumatol. 2017 April ; 36(4): 763–771. doi:10.1007/s10067-016-3515-3.

Cardiovascular Risk Assessment in Patients With Rheumatoid Arthritis: A Correlative Study of Noninvasive Arterial Health Testing

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Abstract

Objectives—This study aimed to determine the relationship between noninvasive measures of arterial health and both estimated 10-year cardiovascular risk and measures of disease activity over time in established rheumatoid arthritis.

Methods—Fifty rheumatoid arthritis patients underwent noninvasive arterial health testing (brachial artery reactivity, aortic augmentation index pulse wave velocity [Aix], carotid artery intima-media thickness, and carotid artery plaque presence) and assessment of clinical disease activity (tender or swollen joint counts, Clinical Disease Activity Index [CDAI], and Health Assessment Questionnaire II [HAQ-II]). Clinical measures during 3 years before the study visit were averaged. Arterial health testing was compared with American Heart Association/American College of Cardiology (AHA/ACC) Pooled Cohort Equation. Spearman methods identified correlations between disease activity measures, cardiac biomarkers, and arterial health parameters.

Results—Among the patients (mean age, 57.5 years), disease activity was moderate (mean [SD] CDAI, 16.9 [15.3]). At the study visit, corrected aortic augmentation index correlated with CDAI ($r=0.37$, $P=.009$) and HAQ-II ($r=0.33$, $P=.02$). Aix correlated with time-averaged tender joint count ($r=0.37$, $P=.008$), CDAI ($r=0.36$, $P=.01$), HAQ-II ($r=0.36$, $P=.01$), swollen joint count ($r=0.36$, $P=.10$), patient global assessment ($r=0.33$, $P=.02$), physician global assessment ($r=0.35$, $P=.01$), and pain score ($r=0.38$, $P=.007$). AHA/ACC low-risk group (<5% 10-year risk) had highest prevalence of carotid plaques.

Conclusions—Arterial health testing may identify increased risk of cardiovascular disease compared with risk obtained through AHA/ACC Pooled Cohort Equation. Measures of arterial stiffness correlate with the burden of disease activity over time.

Keywords

brachial artery reactivity testing; carotid artery intima-media thickness; endothelial dysfunction; flow-mediated dilation; rheumatic disease; swollen joint count; tender joint count

Introduction

Persons with rheumatoid arthritis (RA) have underrecognized silent coronary heart disease that contributes to heightened cardiovascular (CV) death risks (1). Compared with the general population, RA patients have a 50% increased risk of CV-related death (standardized mortality ratio, 1.5 [95% CI, 1.39–1.61]) (1). Risk of atherosclerotic CV disease (ASCVD) in RA patients is underestimated in traditional CV risk scores. The observed CV risk is 2-fold higher than predicted risk by the Framingham score in women and 65% higher in men (2). The Reynolds risk score, which includes C-reactive protein (CRP) and might be predicted to perform better for patients with inflammatory disease, is similarly deficient in estimating CV risk for RA patients (2). Therefore, an unmet need exists for methods to accurately stratify risk of coronary heart disease in persons with RA.

Coronary angiography is the gold standard to identify CV plaque; however, it does not estimate CV risk accurately in the RA patient (3,4). Noninvasive CV imaging can be used to detect early ASCVD in RA patients and can redefine risk in this population, allowing clinicians to identify CV risk and decrease it with an intervention (eg, aspirin). Arterial tonometry and ultrasonography are noninvasive tests that require no radiation and are relatively inexpensive. They measure early endothelial dysfunction, a precursor to clinically identifiable atherosclerotic disease (3). Kullo and Malik (5) highlighted use of high-resolution ultrasonography to measure endothelial function by assessing arterial dilation in response to pharmacologic stimuli (often impaired in plaque formation). They identified several methods useful in measuring arterial stiffness, including aortic pulse wave velocity (aPWV) and aortic augmentation index (AIx). Carotid artery intima-media thickness (CIMT) can be used in asymptomatic patients to measure vascular age and can be an important predictor of heart disease and stroke (6). The Multi-Ethnic Study of Atherosclerosis showed that both carotid plaque and CIMT identified with ultrasonography can independently predict CV events and can improve risk estimates of CV events when applied to Framingham risk factors (6). Stein (7) found that replacing chronological age with vascular age identified with CIMT would reclassify 50% of patients initially placed in the *intermediate risk* category to a different risk category.

RA patients often have less regular screening for traditional CV risk factors such as lipids, smoking, and hypertension—modifiable factors often overlooked because of the complexity of rheumatologic clinical care (1,2,8). The goal of joint endeavors in cardiorheumatology clinical practice is to ameliorate the increased morbidity and mortality rates due to CV disease among persons with rheumatic disease, through implementing improved CV risk assessment and treatment strategies (5,9).

The present study's primary objective was to evaluate RA patients using an innovative, noninvasive arterial health testing panel developed at our institution. The panel includes

measurement of endothelial function (reactive hyperemia and flow-mediated dilation [FMD]), arterial stiffness (aPWV and AIx), and early atherosclerosis (CIMT and carotid plaque presence) to reveal subclinical atherosclerotic disease. Our primary hypothesis was that our innovative arterial health testing package would identify early ASCVD risk not reflected in RA disease measures or through traditional CV risk scoring. Our secondary objective was to determine the relationship between noninvasive arterial health measures and measures of current and average disease activity over time among patients with established RA. We tested for statistically significant differences in the arterial health measures and the categories of low, intermediate, and high risk identified by the American Heart Association (AHA)/American College of Cardiology (ACC) Pooled Cohort Equation (10-year risk %) to learn whether we could identify early CV disease in patients typically classified as being at low or intermediate risk.

Methods

Patients

Fifty patients aged 40 to 65 years fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA and had no history of known ASCVD (ie, coronary artery disease, angina, myocardial infarction, or stroke) or equivalent (eg, diabetes mellitus). Duration of RA from diagnosis was 3 months and 10 years; current treatment with 1 disease-modifying antirheumatic drugs (DMARDs) was 3 months.

Study Design

An electronic database was used to identify potential study participants with an *International Classification of Diseases, Ninth Revision*, code for RA who had an upcoming appointment in the Division of Rheumatology at Mayo Clinic in Rochester, Minnesota, during recruitment from July 1 to November 13, 2016. Using a telephone script approved by the Mayo Clinic Institutional Review Board, the study coordinator (Z.K.) invited patients to participate in the study. The coordinator facilitated a research appointment for patients undergoing rheumatologic assessment by a clinical rheumatology investigator (E.M.S.). This assessment included physical examination of joints and assessment of patient- and provider-derived outcomes. All patients provided written informed consent for study participation, which was approved by the institutional review board and in accordance with the Declaration of Helsinki.

Clinical Assessment

Clinical data were collected during a rheumatologic appointment. These included tender joint count (TJC), swollen joint count (SJC), pain score, Disease Activity Score 28 using CRP (DAS28-CRP), Clinical Disease Activity Index (CDAI), and Health Assessment Questionnaire II (HAQ-II) (2,8).

The patients also had a clinical appointment with the cardiologist co-investigator (R.M.) on the day of the rheumatologic assessment. ASCVD risk score was calculated using the AHA/ACC Pooled Cohort Equation (2,8), which estimates 10-year CV risk as *low* (<5%),

intermediate (5% to <7.5%), and *high* (7.5%). The patient's traditional risk factors, fasting lipid levels, body composition, lifestyle factors, and any metabolic syndrome features were assessed, and on the basis of the risk factor profile, decisions were made to proceed with further CV imaging or follow-up cardiology clinic visits.

Laboratory Measurements

A standardized set of fasting blood measurements was performed for each patient. Laboratory measurements were determined at Mayo Clinic in Rochester according to standard procedures. Blood testing included total cholesterol, triglycerides, high-sensitivity CRP, erythrocyte sedimentation rate, glucose, total bilirubin, uric acid, rheumatoid factor (RF), anti-citrullinated protein antibody (ACPA), hemoglobin, leukocytes, apoprotein A1, galectin-3, lipoprotein A2 (LPA2), pentraxin 3, and N-terminal pro-brain natriuretic peptide.

Data Collection and Study Variables

Retrospective chart review was used to collect data on disease activity measures from the 3 years before the study visit. An electronic clinical data capture system enabled collection of TJC and SJC, patient and provider global assessments of disease activity, HAQ-II disability index, and all RA medications, including biologics (eg, adalimumab, certolizumab pegol, etanercept, tocilizumab) and DMARDs (eg, methotrexate, cyclosporine, cyclophosphamide). CV medications were collected, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, β -blockers, diuretics, and calcium channel blockers. Information on hyperlipidemia medication (eg, statins, fish oil) and aspirin use was captured.

Arterial Physiologic Testing With Arterial Health Panel

For each patient, microvascular and conduit artery function in the forearm was assessed with noninvasive high-resolution ultrasonography of the brachial artery, using a hand-held ultrasound probe (5,10). FMD, a biomarker for endothelial function, was evaluated with high-resolution ultrasonography (10). Ultrasonography of brachial artery reactivity was performed with the International Brachial Artery Reactivity Task Force guidelines using a 10-MHz linear array transducer (5,10) (Acuson Sequoia; Siemens AG). Baseline brachial artery diameter and flow measurements were obtained as previously described (5,10). Conduit artery function was assessed of FMD (endothelium-dependent response) and nitroglycerine-mediated dilation (endothelium-independent response) (5,10).

Aortic Pulse Wave Velocity

Stiffening of the aorta and its major branches can reduce the normal elastic gradient between arterial tree segments; therefore, the common carotid and femoral arteries are used to estimate aPWV because they extend the length of the aorta, which is most prone to stiffening (5,10). In healthy adults, aPWV ranges from 5 to 7 m/s². The aPWV was measured with applanation tonometry as previously described (5,10).

Pulse Wave Analysis

Aortic augmentation pressure reflects the degree of augmentation by central systolic blood pressure in the pressure wave (5,10,11). AIx is a fraction of the central pulse pressure and

reflects interaction between the arterial tree and the left heart ventricle (10,11). It is the difference between first and second systolic peaks of the ascending aortic pressure waveform indexed to central pulse pressure (5,10,11). Use of pulse wave analysis to provide information about hemodynamics has been described previously (5,10,11).

Ultrasonography for CIMT Assessment

A limited carotid ultrasonography examination was performed to measure common CIMT; assessment for flow-limiting obstruction was not performed. CIMT was compared with the 75th percentile for patient age and sex. The methods were described previously (12,13). The areas assessed in 2-dimensional view included the right common carotid posterior wall mean intima-media thickness, posterior wall maximal intima-media thickness, and left common carotid artery posterior wall mean intima-media thickness (12,13). Plaque presence was evaluated in the bilateral common carotid arteries, internal carotid arteries, and carotid artery bulbs, classified as *mild*, *moderate*, or *severe*. A weighted plaque score was obtained by counting the sites where plaque was visible and dividing that number by total sites with images available.

Statistical Methods

Time-averaged measures of disease activity were obtained by averaging daily values obtained through linear interpolation between clinical visits from the earliest visit within 3 years to the study visit. Correlation coefficients between rheumatologic disease activity scores and arterial health testing parameters were obtained using Spearman methods. Heat maps depict correlations between study visit disease activity measures (both study visit and time-averaged measures) and arterial health testing parameters. Statistical significance was defined as $P < .05$. Analyses were performed using SAS version 9.4 (SAS Institute Inc) and R version 3.1.1 (R Foundation for Statistical Computing).

Results

Baseline Characteristics

Of the 50 patients, median age was 57.5 years; median RA disease duration, 6.4 years; and female sex, 38 patients (76%) (Table 1). At the study visit, 16 patients (32%) were taking prednisone; 31 (62%), methotrexate; 21 (42%), other DMARDs; 15 (30%), tumor necrosis factor biologics; and 18 (16%), non-tumor necrosis factor biologics (Table 2). Overall disease activity was moderate (median CDAI, 10.9). Median 10-year CV risk was 4.0% (range, 0.4%–20.3%). Overall, 12 patients (24%) were taking antihypertensive medications (7, angiotensin-converting enzyme inhibitors; 5, angiotensin receptor blockers). Seventeen patients (34%) took antilipid agents.

Comparison of Noninvasive Arterial Health and CV Risk

Comparison of arterial health parameters with estimated 10-year CV risk showed significant associations (Table 2). Hyperemic forearm flow was significantly associated with AHA/ACC risk categories, with lowest median (interquartile range [IQR]) velocity in the low-risk category at 459 (280–565) mL/min; highest median velocity (IQR) in high-risk category was 712 (487–882) mL/min ($P = .048$). No statistically significant correlation was

found between arterial stiffness and CV risk. The results show significant associations between mean and maximal CIMT and estimated CV risk. For example, mean CIMT ranged from a median (IQR) of 0.7 (0.6–0.7) mm in the low-risk category to 0.9 (0.8–1.0) mm in the high-risk category ($P=.01$). Prevalence of carotid plaques did not differ between risk groups ($P=.40$), but 48% of patients in the AHA/ACC low-risk category had carotid plaques (generally mild in severity). One plaque in each of the low and intermediate groups was graded as severe.

Correlations Between Arterial Health Measures and Clinical Disease Activity Parameters

Statistically significant correlations of moderate magnitude were found between multiple RA disease activity parameters at the study visit and arterial stiffness variables, particularly the corrected AIx (Figure 1). Corrected AIx correlated well with DAS28-CRP ($r=0.38$, $P=.007$), CDAI ($r=0.37$, $P=.009$), and other individual clinical disease activity parameters (Figure 1). aPWV correlated with the patient global assessment ($r=0.30$, $P=.04$) but not with other disease activity measures.

Analysis of brachial artery reactivity measures showed that artery diameter correlated inversely with RA disease activity parameters, such as pain score ($r=0.35$, $P=.01$) (Figure 1). In clinical context, brachial artery diameter is associated with presence and amount of coronary artery calcium (10). No significant correlations were observed between FMD, baseline, or hyperemic forearm blood flow and RA clinical disease activity.

Moderate correlations were not statistically significant between mean CIMT, CDAI, and SJC. No significant associations were found between carotid plaque and RA disease activity measures. RA duration did not significantly correlate with any of measures of arterial health.

Correlations Between Arterial Health Measures and Time-Averaged Disease Activity

Relationships between arterial health and the burden of RA disease activity over time were analyzed with time-averaged disease activity measures. Median (range) number of visits was 2.2 (0–3.7); time-averaged CDAI, 11.3 (0.1–47.0); and HAQ-II disability index, 0.6 (0.2–1.2).

In concordance with analysis done at the study visit, the strongest correlations were between corrected aortic augmentation and time-averaged measures of disease activity (Figure 2). Correlation between corrected AIx and time-averaged CDAI was the same as with HAQ-II disability index: 0.36 ($P=.01$). Correlation coefficients for the association between corrected AIx and TJC, SJC, patient global assessment, provider global assessment, and pain score ranged from 0.33 to 0.38 (all $P<.02$). Modest correlations were observed between aPWV but were not statistically significant.

Similar to the analysis at the study visit, these analyses revealed inverse correlations between brachial artery diameter and both time-averaged patient global assessments ($r=0.30$, $P=.03$) and pain score ($r=0.35$, $P=.01$). Brachial artery diameter was not correlated with CDAI ($r=0.16$, $P=.28$). No significant associations were observed between FMD and any RA parameter. Regarding carotid ultrasonography, no meaningful correlations were found

between mean common CIMT or plaque and time-averaged disease activity measures (Figure 2).

Adjusted Correlations Between AIx and Time-Averaged CDAI

A multivariable analysis examined the association between AIx and time-averaged CDAI (Table 3). The unadjusted correlation between the corrected AIx and the CDAI was 0.36 ($P=.01$). Adjustment for the AHA/ACC CV risk score revealed a stronger correlation ($r=0.41$, $P=.007$). Further adjustment for use of prednisone, methotrexate, or biologics attenuated the correlation between AIx and time-averaged CDAI ($r=0.3$, $P=.07$).

Correlations Between Biomarkers and Arterial Health Measures

Various biomarkers correlated with brachial artery parameters (Figure 3). LPA2 correlated strongly with artery diameter ($r=0.48$, $P<.001$), baseline forearm blood flow ($r=0.50$, $P<.001$), and hyperemic blood flow ($r=0.39$, $P=.009$). Similarly, triglycerides correlated strongly with baseline forearm blood flow ($r=0.48$, $P<.001$) and hyperemic blood flow ($r=0.45$, $P=.001$). High-density lipoprotein cholesterol correlated negatively with brachial artery diameter ($r=-0.29$, $P=.04$), baseline forearm flow ($r=-0.40$, $P=.004$), and hyperemic forearm blood flow ($r=-0.42$, $P=.002$). A similar pattern of correlation coefficients was observed for apoprotein A1, albeit weaker and nonsignificant. Brachial artery diameter correlated with results positive for ACPA ($r=0.36$, $P=.01$). Finally, high-sensitivity CRP was also associated with baseline ($r=0.34$, $P=.02$) and hyperemic forearm blood flow ($r=0.31$, $P=.03$).

Regarding arterial stiffness measures, aPWV correlated with low-density lipoprotein cholesterol ($r=0.37$, $P=.008$) and LPA2 ($r=0.30$, $P=.04$) (Figure 3). N-terminal pro brain natriuretic peptide correlated with both AIx ($r=0.38$, $P=.009$) and corrected AIx ($r=0.33$, $P=.03$).

LPA2 again showed moderate association with mean CIMT and low correlation with the presence of carotid plaques. High-density lipoprotein cholesterol showed negative correlations with the mean common CIMT. Plaque presence did not correlate with any biomarker.

Discussion

A goal of the cardiorheumatology discipline is to understand how to best estimate the CV disease risk for RA patients so risk modification strategies can be undertaken to improve survival from ASCVD (14). Early ASCVD risk management can include preemptive initiation of statin therapy, but interestingly, no guideline has been identified for CV prevention in patients with inflammatory joint disease (9). The observational study by Rollefstad et al (9) provides a model of how to approach early CV disease identified in RA patients through ultrasonography, because the researchers identified a high frequency of carotid plaques in RA patients, leading to early initiation of statin use.

The present study showed that RA-related disease activity at baseline and averaged over 3 years is associated with increased arterial stiffness, as defined by corrected AIx and aPWV. To our knowledge, this is the first study to compare time-averaged disease activity and

markers of noninvasive arterial health. Other studies previously have identified that the FMD percentage is greater among patients with high inflammatory activity, which was not identified in our study at the study visit or at the time-averaged activity measures (15,16). The discordant findings in the present study could be related to the small sample (N=50) (16).

This study compared arterial health testing and AHA/ACC estimated 10-year CV risk. Of interest, plaque was present in 48% of the low-risk group and 57% of the intermediate-risk group, thus suggesting that noninvasive arterial health testing may identify early plaque presence in patients who normally would be categorized in the low- or intermediate-risk group. Semb et al (17) showed that evidence of asymptomatic carotid plaques would reclassify patients into a more appropriate CV risk category (European Society of Cardiology Systematic Coronary Risk Evaluation [SCORE] and AHA/ACC risk calculators).

Statistically significant correlations arose between the study visit and arterial stiffness, particularly the corrected AIx but also aortic augmentation pressure and aPWV. This association was shown by Klocke et al (18), who found AIx as a measure of arterial stiffness varied in RA patients versus controls without RA. aPWV is a surrogate marker for arterial stiffness, which has been studied extensively by Malik et al (15) and Klocke et al (18) and has been found by other investigators (eg, Ambrosino et al [19]) to be abnormal in highly inflammatory states. At the study visit, no associations between carotid plaque and RA disease activity were identified. Similar to the results of analyses at study visit, analysis of time-averaged measures of disease activity revealed strong correlations between the corrected AIx and time-averaged measures of disease activity. This finding is suggestive that measures of disease activity, such as TJC, SJC, and provider global assessment, and pain score could affect arterial stiffness. Interestingly, adjustment for medication use diminished the correlation between AIx and time-averaged CDAI.

Biomarker analysis suggested that LPA2 correlated with brachial artery diameter and baseline forearm blood flow and showed moderate association with mean CIMT and low correlation with presence of carotid plaques. This relationship has been identified in other studies. LPA2 measurement has been reported as potentially useful for stratifying CV risk (20); in animal models, increased LPA2 has been associated with atherogenesis (21).

Strengths

The study setting of a dedicated cardiorheumatology clinic as a joint clinical practice and with the goal to address the high ASCVD risk in patients with autoimmune rheumatic disease is a unique collaborative care model (22). Unlike previous studies that typically assessed only 1 CV risk parameter (eg, endothelial function, CIMT), multiple measures of early CV risk were used in this study to assess for early atherosclerosis (23). The arterial health testing package was an innovative tool that included all potential noninvasive variables that may be expected to be abnormal, translated to a clinical setting.

Limitations

The study's generalizability may be limited because it was conducted at a tertiary referral center that evaluates global patients and complex RA cases (14,24). Fewer male patients were in the study than female patients, although the proportion of women (76%) is representative of the RA population (24). Patients had had moderate overall disease activity (CDAI, 10.9). CRP was not routinely measured in the study visits over the time extracted from medical charts, and therefore CDAI score and HAQ-II score were used with assessment of arterial health measures.

Conclusion

These study findings showed a significant relationship between markers of arterial stiffness (corrected AIx), atherosclerosis (CIMT), and disease activity at both the study visit and time-averaged measures over 3 years. Correlations between arterial health measures and disease activity support previous findings that RA disease activity affects ASCVD development. Early plaque formation was noted even for patients who would be characterized as low and intermediate risk in the AHA/ACC Pooled Cohort Equation. In addition, the biomarkers identified a strong correlation between LPA2 and brachial artery parameters. Future studies could evaluate CV risk in new-onset RA and serially assess progression of arterial stiffness and CV risk over time using the arterial health testing package in the context of RA disease activity. Information gained could provide patients and physicians with useful guidance for both RA disease management and CV disease prevention and management.

Acknowledgments

This project was supported by the 2015 Mayo Clinic Department of Medicine Team Science Award, Grant Number R01 AR46849 from the National Institute for Arthritis Musculoskeletal and Skin Diseases (NIAMS), and CTSA Grant Number UL1 TR000135 from the National Center for Advancing Translational Science (NCATS). Its content are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health.

The study sponsors had no role in the study design; collection, analysis, or interpretation of the data; in the drafting of the manuscript; or in the decision to submit the manuscript for publication.

Abbreviations

AIx	aortic augmentation index
ACC	American College of Cardiology
AHA	American Heart Association
ACPA	anti-citrullinated protein antibody
aPWV	aortic pulse wave velocity
ASCVD	atherosclerotic cardiovascular disease
CDAI	Clinical Disease Activity Index

CIMT	carotid artery intima-media thickness
CRP	C-reactive protein
CV	cardiovascular
DAS28-CRP	Disease Activity Score 28 using C-reactive protein
DMARD	disease-modifying antirheumatic drug
FMD	flow-mediated dilation
HAQ-II	Health Assessment Questionnaire II
IQR	interquartile range
LPA2	lipoprotein A2
RA	rheumatoid arthritis
RF	rheumatoid factor
SJC	swollen joint count
TJC	tender joint count

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Figure 1.

Correlations Between Study Visit Disease Activity Measures and Noninvasive Arterial Health Testing Measures. Heat map shows the magnitude of Spearman correlation coefficients. Blue indicates a positive association; red, a negative association. CDAI indicates Clinical Disease Activity Index; HAQ-II, Health Assessment Questionnaire II.

Figure 2.

Correlations Between Time-Averaged Disease Activity Measures and Noninvasive Arterial Health Testing Measures. Heat map shows the magnitude of Spearman correlation coefficients. Blue indicates a positive association; red, a negative association. CDAI indicates Clinical Disease Activity Index; HAQ-II, Health Assessment Questionnaire II.

Figure 3. Correlations Between Biomarkers and Measures of Noninvasive Arterial Health Testing. Heat map shows the magnitude of Spearman correlation coefficients. Blue indicates a positive association; red, a negative association. NT indicates N-terminal.

Table 1**Baseline Characteristics of 50 Patients With RA**

Characteristic	Value ^a
Age, y	57.5 (52.8–61.6)
Female sex	38 (76)
White race	48 (96)
Systolic blood pressure, mm Hg	123 (111–133)
Diastolic blood pressure, mm Hg	76.5 (67–84)
Body mass index, kg/m ²	27.9 (23.9–34.9)
RA disease duration, y	6.4 (3.8–9.7)
Medication use	
Prednisone	16 (32)
Methotrexate	31 (62)
TNF inhibitor	15 (30)
Tender joint count (0–28)	2.0 (0.0–14.0)
Swollen joint count (0–28)	2.0 (0.0–7.0)
HAQ-II disability index (0–3)	0.6 (0.2–1.3)
Pain (0–100 mm)	28.5 (13.0–50.0)
Patient global assessment (0–100 mm)	27.0 (10.4–47.0)
Physician global assessment (0–100 mm)	30.0 (5.0–60.0)
DAS28-CRP	3.0 (2.4–4.8)
CDAI	10.9 (5.0–31.0)
AHA/ACC Pooled Cohort Equation 10-y ASCVD risk, %	4.0 (1.5–6.6)
Anti-CCP, positive	28 (57.1)
Rheumatoid factor, positive	32 (64.0)
Lipids, mg/dL	
Total cholesterol	184.5 (167.0–212.0)
Triglycerides	104.5 (78–143.0)
HDL-C	62.0 (44.0–76.0)
LDL-C	98.5 (85.0–118.0)
hs-CRP, mg/L	2.4 (1.0–5.3)
Sedimentation rate, mm/h	9.5 (4.0–17.0)

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; anti-CCP, cyclic citrullinated peptide antibody; ASCVD, atherosclerotic cardiovascular disease; CDAI, Clinical Disease Activity Index; DAS28-CRP, Disease Activity Score 28 using C-reactive protein; HAQ-II, Health Assessment Questionnaire II; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; RA, rheumatoid arthritis; TNF, tumor necrosis factor.

^aValues represent either median and interquartile range or number and percentage of patients.

Table 2

Results of Noninvasive Arterial Health Testing of 50 Patients With Rheumatoid Arthritis

Parameter	AHA/ACC Pooled Cohort Equation, ^a 10-y risk %				P Value
	<5.0 (n=29)	5.0–<7.5 (n=7)	7.5 (n=8)	Total	
Brachial artery reactivity testing					
Diameter, mm	3.6 (3.1–3.7)	3.3 (3.2–4.5)	3.9 (3.5–4.5)	3.6 (3.1–3.9)	.40
Flow-mediated dilatation, %	10.3 (7.5–13.3)	9.5 (3.1–12.0)	6.1 (5.1–10.8)	9.6 (5.7–12.1)	.42
Baseline forearm blood flow, mL/min	65 (46–92)	118 (20–148)	121.5 (80–184)	81 (46–123.5)	.10
Hyperemic forearm blood flow, mL/min	459 (280–565)	539 (232–751)	712 (487–882)	471 (280–595)	.048
Arterial stiffness					
Central aortic pressure, mm Hg	1.5 (1.4–1.7)	1.6 (1.5–1.7)	1.5 (1.4–1.7)	1.5 (1.4–1.7)	.95
Pulse pressure, mm Hg	40 (31–49)	44 (40–48)	37 (34–49)	40.5 (33–48.5)	.79
Aortic augmentation pressure, mm Hg	12 (9–15)	17 (9–19)	9.5 (7–18)	12 (8.5–18)	.73
Aortic pulse wave velocity, mm/s	8.2 (7.7–9.0)	8.6 (7.7–9.2)	9.4 (8.1–11.4)	8.2 (7.7–9.8)	.32
Alx	30 (27–36)	35 (25–45)	29 (21.5–34.5)	29.5 (25.5–37)	.54
Corrected Alx	25 (19–33)	31 (19–33)	24 (19.5–30.5)	25 (19–33)	.86
Carotid ultrasonography					
Mean CIMT, mm ^b	0.7 (0.6–0.7)	0.8 (0.7–0.9)	0.9 (0.8–1.0)	0.7 (0.7–0.8)	.01
Maximal CIMT, mm ^c	0.8 (0.7–0.9)	0.9 (0.8–1.1)	1.0 (0.9–1.2)	0.8 (0.8–0.9)	.02
Presence of carotid plaques	14 (48)	4 (57)	2 (25)	20 (46)	.40
Severity of carotid plaques ^d					.03
Mild	13 (93)	3 (75)	1 (50)	17 (85)	
Moderate	0 (0)	0 (0)	1 (50)	1 (5)	
Severe	1 (7)	1 (25)	0 (0)	2 (10)	

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; Alx, aortic augmentation index; CIMT, common carotid intima-media thickness.

^aValues are either median and interquartile range or number and percentage of patients.^bMissing for 6 patients.^cMean of right and left.^dAmong patients with plaques.

Table 3

Correlations Between Time-Averaged Clinical Disease Activity Index and Corrected Aortic Augmentation Index

Model	Spearman Correlation Coefficient	P Value
Unadjusted	0.36	.01
Adjusted for pooled cohort CV risk score	0.41	.007
Adjusted for pooled cohort CV risk score and use of prednisone, methotrexate, and/or biologics	0.30	.07

Abbreviation: CV, cardiovascular.