Metabolic cardiovascular risk burden and atherosclerosis in African black and Caucasian women with rheumatoid arthritis: a cross-sectional study

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Abstract

Objectives

The impact of metabolic risk factors on atherosclerotic cardiovascular disease (ACVD) in patients with rheumatoid arthritis (RA) from developing populations is currently unknown. We examined the relationships of the metabolic syndrome (MetS) and its components with carotid artery atherosclerosis in African women with rheumatoid arthritis (RA) from a developing black and developed Caucasian population.

Methods

We assessed the associations of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) defined MetS and its criteria with high resolution B-mode ultrasound determined common carotid artery intima-media thickness (cIMT) and carotid artery plaque in multivariable regression models in 104 black and 93 Caucasian women with RA.

Results

The MetS prevalence was 30.8% in black compared to 9.7% in Caucasian women with RA (adjusted odds ratio [95% confidence interval]=10.11 [1.76–58.03] [p=0.009]). Population origin impacted on the relationships of metabolic risk factors with atherosclerosis. In Caucasian women, the MetS was associated with cIMT (p=0.036) and MetS triglycerides and the number of MetS criteria were each associated with both cIMT (p=0.01 and p=0.028, respectively) and plaque (p=0.049 and p=0.02, respectively); by contrast, in black women, MetS blood pressure was related to cIMT (p=0.04).

Conclusion

A high overall metabolic cardiovascular risk burden as disclosed by markedly prevalent MetS in women with RA from developing groups of black African descent was not associated with atherosclerosis. This calls for systematic rigorous cardiovascular risk management irrespective of metabolic risk factor profiles in African black women with RA.

Key words

metabolic syndrome, rheumatoid arthritis, developing population

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that doubles the risk for atherosclerotic cardiovascular disease (ACVD) events (1). ACVD death rates are increased by 50% and account for most of the excess overall mortality in RA (2).

Conventional and non-conventional cardiovascular risk factors or RA characteristics and genetic polymorphisms are associated with ACVD in RA (3-15). Additionally, the RA characteristics of disease activity and treatment with traditional disease modifying drugs, biological agents and corticosteroids can impact on the metabolic syndrome (MetS) and its features including insulin resistance, visceral adiposity and circulating lipid concentrations (16-26). We and others have recently reported that metabolic risk factors are independently associated with both carotid and coronary artery atherosclerosis in RA (18, 20, 27).

Our knowledge on atherogenesis in RA originates almost exclusively in developed populations (28, 29). However, developing populations are not immune to RA (29) and ~80% of ACVD now arises in middle and low income or developing countries (28) in which ACVD risk factor profiles and their impact on atherogenesis are dissimilar (29, 31, 32). Optimal strategies in ACVD risk assessment and prevention in patients with RA from developing populations await delineation.

South Africa is a sub-Saharan country that has become the most unequal society in the world (33). A minority of its inhabitants represents an overall affluent, developed and mostly African Caucasian population, whereas the majority is socially and economically disadvantaged, at an earlier epidemiological health transition stage with consequent different cardiovascular risk factor profiles and disease presentation and consists mostly of an African black population (32, 34, 35). A distinctly high prevalence of obesity that further impacts substantially on blood pressure and glucose and lipid metabolism has been increasingly documented particularly in black South African women (36, 37). Despite this, ACVD event rates remain distinctly low in black Africans (32, 34) with ischemic heart disease currently being confirmed in only 6% of South African black patients that present to hospital with heart disease (38). These findings suggest that in populations that are at an earlier epidemiological health transition stage, metabolic cardiovascular risk factors may not as yet translate into atherosclerosis. Furthermore, whether this apparent lack of association between metabolic cardiovascular risk and ACVD is present in persons from developing populations that have RA, is currently unknown.

The MetS is a multidimensional risk factor for ACVD and diabetes (39). The US National Cholesterol Education Program (NCEP) describes the MetS as the metabolic complications of obesity (39). In the present study, we examined whether or not disparities exist between the relationships of the NCEP-MetS and its individual components with ultrasonographically determined carotid atherosclerosis (18, 27, 40, 41) in women with RA from a developing black compared to a developed Caucasian population.

Materials and methods

Study populations

Study participants comprised consecutively recruited African black and Caucasian women with RA (42, 43) at the Charlotte Maxeke Johannesburg Academic Hospital (public healthcare) and Milpark Hospital (private healthcare) in Johannesburg. None of the data were previously reported. Only 13 African black men with RA participated and, hence, to avoid confounding of the data analysis by gender differences, our research question was addressed in women only. We included women that had used disease modifying agents and, therefore, had established RA. Four invited patients refused to participate and those known to be infected with Human Immunodeficiency Virus (HIV) were excluded. Whereas HIV infection status is currently systematically recorded in our African black patients with patient refusal rates of ~1%, this is not done routinely in our Caucasian patients in view of the distinctly low

prevalence of HIV infection in such subjects. The study was approved by Ethics Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand. Written informed consent was obtained from each patient.

Assessments

Using methods as previously reported by us (18, 29, 35, 43, 44), we assessed sociodemographic characteristics, lifestyle factors, body mass index (BMI), systolic and diastolic blood pressure, diabetes mellitus status, RA characteristics, markers of systemic inflammation including the erythrocyte sedimentation rate (ESR) and serum C-reactive protein concentrations (CRP) and other potential cardiovascular risk factors comprising years of education, the Arthritis Impact Measurement Scales (AIMS) depression score, thyroid status and hormone replacement therapy. Exercise included hours spent in walking (*e.g.* to reach public transport). Data were missing in less than 5% of any of the recorded variables. Serum lipid and plasma glucose concentrations were determined on fasting blood samples and using standard laboratory methods (18, 29, 35, 43, 44).

B.A. Stevens (BAS) (see *Acknowledgement*) and A. Solomon (AS) performed the carotid artery ultrasound measurements in private and public healthcare patients, respectively. Both operators obtained images of at least 1cm length of the distal common carotid arteries for measurement of the intima-media thickness of the far wall from an optimal angle of incidence defined as the longitudinal angle of approach where both branches of the internal and external carotid artery are visualised simultaneously (45) and with high resolution B-mode ultrasound (Image Point, Hewlett Packard, Andover, MA, USA and SonoCalc IMT, Sonosite Inc, Bothell, Wash, USA used by BAS and AS, respectively) employing linear array 7.5 MHz probes. The details of the methodology used by BAS were reported previously (3). The equipment used by AS involves the application of a unique semi-automated border detection programme that was previously found to provide highly reproducible results (45). The intima-media thicknesses in the left and right common carotid artery were measured and the carotid intima-media thickness (cIMT) was defined as the mean of these. Carotid artery plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness value, or demonstrates a thickness of >1.5 mm as measured from the media-adventitia interface to the intima-lumen interface (46). Both operators were blinded to the cardiovascular risk profiles of the patients. Repeat ultrasound examinations by both operators on 23 patients revealed Spearman correlations between repeat cIMT measurements of 0.983 and 0.956 for BAS and AS, respectively, and the correlation between measurements made by BAS and AS was 0.926. Both operators identified carotid artery bulb or/and internal carotid artery plaque in 11 of these 23 patients with full agreement.

We classified patients as having the NCEP-MetS using the criteria as updated by the American Heart Association and the National Heart, Lung and Blood Institute in 2005 (39). The NCEP identifies women as having the MetS when 3 or more of the following criteria are present: a) waist circumference ≥88 cm; b) triglycerides ≥1.7 mmol/l or drug treatment for elevated triglycerides; c) HDL-cholesterol <1.3 mmol/l or drug treatment for reduced HDL-cholesterol; d) systolic blood pressure ≥130 mm Hg or/and diastolic blood pressure ≥85 mm Hg or drug treatment for hypertension; and e) fasting glucose >5.5 mmol/l or drug treatment for elevated glucose.

Statistical analysis

Continuous variables are reported as mean (SD) and dichotomous variables as proportions or percentages. Non-normally distributed characteristics were logarithmically transformed prior to statistical analysis and for these variables geometric means (SD) are given. Differences in sociodemographic features between black and Caucasian Africans were compared using the Student *t*-test and univariate logistic regression analysis as appropriate. Relationships between population grouping (PG) and baseline characteristics, the cIMT and carotid artery plaque and the metabolic syndrome and its components as well as the associations of the MetS definition with baseline characteristics in black and Caucasian women with RA were investigated in multivariable logistic and linear regression models as appropriate and with consistent adjusting for age and healthcare centre attendance.

To determine whether there were disparities in the relationships of metabolic risk factors with atherosclerosis in African black compared to Caucasian patients, we assessed the associations of interactions between PG and the respective risk factors with cIMT and plaque in age, healthcare centre and individual term adjusted multivariate regression models and, subsequently, performed stratified analysis.

Statistical computations were made using the GB Stat™ programme (Dynamic Microsystems, Inc, Silverspring, Maryland, USA).

Results

Baseline characteristics and atherosclerosis in African black compared to Caucasian women with RA

Baseline characteristics and carotid artery atherosclerosis in African Caucasian and black women with RA are shown in Table I. Black women were on average 1.9 years younger (p=0.2) than Caucasian women. Approximately 97% of black women and 83% Caucasians were seen in public and private care, respectively (p<0.0001). As compared to their Caucasian counterparts and in sociodemographic characteristic adjusted analysis, black women with RA had a smaller pack year history smoking, used alcohol less often and had a higher BMI and lower serum total and HDL cholesterol concentrations but similar total cholesterol÷HDL cholesterol ratios, a higher ESR and lower educational level. The atherosclerosis burden was similar in black and Caucasian patients with RA. Antihypertensive medications, oral glucose lowering agents, insulin, statins and ezetimibe were used in 43.0 and 54.8

Table I. Recorded characteristics in African Caucasian and black women with RA.

Characteristics	Caucasian women (n=93)	Black women (n=104)	*p*-value*
Sociodemographics			
Age, years	57.3 (11.8)	55.4 (10.0)	…
Public healthcare (%)	16.7	96.6	…
Lifestyle factors			
Pack year history smoking†, n	2.5 (4.0)	0.1 (1.5)	0.002
Alcohol use (%)	34.8	1.9	<0.0001
Exercise, hours per week†, n	0.7 (2.1)	1.6 (1.9)	0.01
BMI, kg/m^2	25.4 (4.9)	30.0 (6.6)	0.0008
Blood pressure			
Systolic blood pressure, mm Hg	129 (17)	140 (24)	0.8
Diastolic blood pressure, mm Hg	78 (9)	85 (14)	0.2
Lipids			
Total cholesterol, mmol/l	5.1 (1.0)	4.7 (0.9)	0.03
LDL cholesterol, mmol/l	2.8 (0.9)	2.6 (0.8)	0.5
HDL cholesterol†, mmol/l	1.7 (1.3)	1.5 (1.3)	0.002
Total cholesterol÷HDL cholesterol	3.1 (1.0)	3.3 (1.1)	0.1
Triglycerides†, mmol/l	1.1 (1.5)	1.1 (1.7)	0.9
Triglycerides÷HDL cholesterol†	0.6 (1.8)	0.7 (2.1)	0.1
Non-HDL cholesterol	3.3 (1.0)	3.2 (1.0)	0.1
Diabetes mellitus (%)	4.3	17.3	0.5
RA characteristics			
Disease duration, years	14.6 (8.7)	12.9 (9.2)	0.9
Rheumatoid factor positive (%)	73.9	76.0	1.0
DAS28	3.5 (1.5)	4.2 (1.3)	0.5
Deformed joints†, n	3 (4)	7 (3)	0.1
Prednisone ever (%)	41.9	43.3	0.2
Current DMARD, n	2.1 (1.0)	2.5 (1.0)	0.3
Current methotrexate use (%)	78.5	92.3	0.7
Current chloroquine use (%)	46.2	77.9	0.1
Systemic inflammation			
Erythrocyte sedimentation rate†, mm/hr	7 (3)	21 (3)	0.007
C-reactive protein†, mg/l	3.8 (3.5)	7.5 (3.1)	0.2
Other			
Education, years	12.8 (2.7)	7.5 (4.1)	0.002
AIMS depression†	1.9 (1.8)	3.3 (1.6)	0.07
Hypothyroidism‡ (%)	35.5	5.8	0.1
Hormone replacement therapy (%)	18.3	5.8	0.9
Atherosclerosis			
CIMT, mm	0.689 (0.118)	0.691 (0.096)	0.7
Plaque (%)	35.5	35.6	0.2

Results are expressed as mean (SD) unless indicated otherwise.
*p-value for comparisons between African black and Caucasian women after adjustment for age and healthcare as well as lipid lowering and antihypertensive agents in models that include lipid and blood pressure variables, respectively. †Non-normally distributed variable for which geometric mean (SD) is given. ‡It includes subclinical and overt hypothyroidism and diagnosed when thyrotropin level was >4.94 mU/L or when thyroid hormone replacement therapy was used. RA: rheumatoid arthritis; BMI: body mass index; DAS28: disease activity score in 28 joints; DMARD: disease modifying agents for rheumatic disease; AIMS: arthritis impact measurement scales; CIMT: common carotid artery intima-media thickness.

(p=0.1), 4.3 and 14.4 (p=0.02), 1.1 and 1.9 (p=0.6), 36.6 and 19.2 (p=0.007) and 2.2 and 0% of Caucasian and black women, respectively.

Metabolic risk factors in African black compared to Caucasian women with RA

The metabolic syndrome characteristics in African black and Caucasian women with RA are shown in Table II. The MetS prevalence was 9.7% in Caucasians and 30.8 % in black women with RA. Each of the individual MetS components was numerically markedly more prevalent in black compared to Caucasian women. In age and healthcare centre attendance adjusted analysis, black women with RA sustained an odds ratio for having MetS HDL cholesterol and meeting sufficient criteria for the NCEP MetS definition of 6.1 and 10.1, respectively. Moreover, the number of metabolic syndrome criteria was significantly larger in black compared to Caucasian Africans with RA.

Characteristics of African black and Caucasian women with RA by MetS status

The characteristics in African black and Caucasian women with RA who had and who did not have MetS are shown in Table III. Sociodemographic characteristics did not significantly differ in both black and Caucasian women with and without the MetS (p≥0.08). In sociodemographic characteristic adjusted analysis, the MetS was associated with the BMI, serum triglyceride and non-HDL cholesterol concentrations and the total cholesterol÷HDL cholesterol and triglyceride÷HDL cholesterol ratios in black and Caucasian women; the MetS was further associated with a high pack year history smoking, systolic and diastolic blood pressure, the DAS28 and AIMS depression score in Caucasian women and with low serum HDL cholesterol concentrations in black women with RA.

Relationships between metabolic risk factors and carotid artery atherosclerosis in African black and Caucasian women with RA

In sociodemographic characteristic adjusted analysis, MetS blood pressure and the number of metabolic syndrome criteria were associated with the cIMT in all African women with RA (standardised [S] β [95% CI]=0.18 [0.04–0.31], p=0.01 and S β=0.14 [0.00–0.35], p=0.04, respectively). The metabolic syndrome and each of its components were not associated with carotid artery plaque in all black and Caucasian women with RA.

Interactions between PG and metabolic syndrome features that were associated with cIMT in all women with RA independent of age, healthcare centre and individual terms comprised PG x the MetS triglycerides (p=0.034) and PG x the MetS definition (p=0.02). Disparities in the relationships of metabolic cardiovascular risk with cIMT in

Table II. Metabolic syndrome criteria in African Caucasian and black women with RA.

MetS characteristics	Caucasian women (n=93)	Black women (n=104)	OR* (95% CI)
MetS waist	33.3	64.7	2.47 (0.92–6.60)
MetS blood pressure	59.1.5	83.7	1.45 (0.45–4.68)
MetS HDL-cholesterol	15.1	21.2	6.14 (1.11–33.92)†
MetS triglycerides	11.8	17.3	0.82 (0.23–2.92)
MetS glucose	5.4	20.2	2.73 (0.52–14.36)
MetS definition	9.7	30.8	10.11 (1.76–58.03)‡
Continuous variable	Caucasian women mean (SD)	Black women mean (SD)	*p*-value*
MetS criteria, n	1.3 (1.0)	2.1 (1.1)	0.03

Dichotomous variables are expressed as proportions or percentages. *Odds ratio and *p*-value for comparisons between African black and Caucasian African women after adjustment for age, sex and healthcare centres. †*p*=0.036. ‡*p*=0.009. RA: rheumatoid arthritis; MetS: metabolic syndrome; HDL: high-density lipoprotein.

black compared to Caucasian women in stratified analysis are shown in Table IV. MetS triglycerides, the MetS definition and the number of MetS criteria were associated with cIMT in Caucasian women, whereas MetS blood pressure was associated with cIMT in black women with RA.

Interactions between PG and metabolic syndrome features that were associated with plaque in all women with RA independent of age, healthcare centre and individual terms comprised PG x the MetS waist (*p*=0.01), PG x the number of Mets criteria (*p*=0.02) and PG x the MetS definition (*p*=0.05). Disparities in the relationships of metabolic cardiovascular risk with plaque in black compared to Caucasian women in stratified analysis are shown in Table V. MetS triglycerides and the number of MetS criteria were associated with plaque in Caucasian women, whereas none of the metabolic risk factors was related to plaque in black women with RA.

Baseline recorded characteristics that are potential non-metabolic risk factors and differed between African black and Caucasian women with RA (Table I) included life style factors (pack year history smoking, alcohol use and exercise), the ESR and years of education. In separate models amongst African Black women with RA and in which age and healthcare centre together with these characteristics were adjusted for, MetS waist, MetS HDL cholesterol, MetS triglycerides, MetS glucose and the MetS definition and number of MetS criteria remained unrelated with cIMT (S β=-0.05, *p*=0.6, S β=0.09, p=0.4, S β=0.03, *p*=0.8, S β=-0.10, *p*=0.3, S β=-0.07, *p*=0.5 and S β=0.06, *p*=0.6, respectively) and plaque (odds ratio [OR] [95% confidence interval CI]=1.02 [0.93–1.11], *p*=0.8 ,OR (95%CI)=0.46 [0.13–1.63], *p*=0.5 ,OR (95% CI)=1.23 [0.36–4.21], *p*=0.8, OR (95%CI)=1.23 [0.39–4.20], *p*=0.7 , OR (95%CI)=0.63 [0.21–1.86], *p*=0.4 and OR [95%CI]=0.78 [0.50–1.24], p=0.3, respectively), whereas MetS blood pressure remained associated with cIMT (S β=0.19, *p*=0.049) and unassociated with plaque (OR [95%CI]=1.97 [0.47–8.24], *p*=0.4).

In patients with RA from developed populations, systemic inflammation can explain the association of metabolic risk with atherosclerosis (20). In additional models amongst Caucasian women with RA in which age and healthcare centre together with the DAS28, C-reactive protein concentrations and the ESR were adjusted for, MetS triglycerides were no longer significantly associated with plaque (OR [95%CI]=4.59 [0.71–29.60], *p*=0.1), but the MetS remained related to cIMT (S β=0.17, *p*=0.05) and the number of MetS criteria was still associated with cIMT (S β=0.21, *p*=0.027) and plaque (OR [95%CI]=2.14 [1.12–4.06], *p*=0.02).

Discussion

In this study, African black women with RA experienced a markedly increased metabolic risk factor burden compared to their Caucasian counterparts. However, although MetS blood pressure was related to cIMT, overall metabolic risk as reflected by the MetS and number of its components were not associated with carotid atherosclerosis in black women with RA. In contrast, overall metabolic risk was consistently related to carotid atherosclerosis independently of sociodemographic characteristics in Caucasian women with RA. As applies to previously reported studies that examined cardiovascular risk in non-RA and RA subjects, many relationships were assessed. However, our main findings were each produced in confounder adjusted multivariable analysis. To our knowledge, this is the first study that simultaneously assessed and directly compared the relationships of metabolic cardiovascular risk with atherosclerosis between patients with RA that belong to a developing and developed population.

African black women with RA used numerically more often antihypertensive agents than their Caucasian counterparts, in the present study. This would appear to further support our observation that MetS blood pressure is associated with carotid atherosclerosis in black but not Caucasian African women with RA, since antihypertensive agents reduce adverse cardiovascular outcomes. However, the association between MetS blood pressure and cIMT in African black women with RA should be interpreted with caution. CIMT and plaque represent different aspects of arterial pathology and are biologically and genetically distinct (47-52). The cIMT constitutes ~80% media and ~20% intima (48). Intima-media thickening results mostly from adaptive responses of medial cells to blood pressure and age and associates mostly with stroke risk factors and stroke, whereas carotid artery plaque arises as a consequence of intimal pathology and reflects an advanced stage of atherosclerosis that is more closely associated with coronary artery disease risk factors and ischemic heart disease prevalence (48-50). Therefore, the most striking and important finding in the present study is the consistent lack of relationships of metabolic cardiovas-

Table III. Recorded characteristics in African Caucasian and black women with RA with and without metabolic syndrome.

Characteristics	Caucasian women			Black women		
	MetS (n=9)	no MetS (n=84)	*p*-value*	MetS (n=32)	no MetS (n=72)	*p*-value*
Sociodemographics						
Age, years	59.2 (14.5)	57.1 (11.5)	…	55.7 (9.5)	55.3 (10.3)	…
Public healthcare (%)	22.2	16.7	…	97.1	90.6	…
Lifestyle factors						
Pack year history smoking†, n	13.3 (5.6)	0.12 (4.7)	0.009	0.1 (1.4)	0.1 (1.5)	0.9
Alcohol use (%)	50.0	33.3	0.4	6.3	0.0	1.0
Exercise, hours per week†, n	0.7 (1.9)	0.5 (2.0)	0.5	0.5 (2.9)	0.8 (2.1)	0.3
BMI, kg/m^2	30.9 (4.5)	24.8 (4.6)	0.0003	32.5 (6.4)	28.9 (6.4)	0.01
Blood pressure						
Systolic blood pressure, mm Hg	150 (17)	126 (16)	<0.0001	141 (23)	139 (24)	0.7
Diastolic blood pressure, mm Hg	85 (13)	77 (8)	0.01	87 (13)	84 (15)	0.3
Lipids						
Total cholesterol, mmol/l	5.7 (1.5)	5.1 (1.0)	0.1	4.8 (1.0)	4.7 (0.8)	0.5
LDL cholesterol, mmol/l	3.0 (1.0)	2.8 (0.9)	0.6	2.7 (0.9)	2.6 (0.7)	0.6
HDL cholesterol†, mmol/l	1.5 (1.5)	1.8 (1.3)	0.1	1.2 (1.3)	1.6 (1.2)	<0.0001
Total cholesterol÷HDL cholesterol	3.9 (1.4)	3.0 (0.9)	0.009	4.1 (1.3)	2.9 (0.7)	<0.0001
Triglycerides†, mmol/l	2.1 (1.7)	1.0 (1.4)	<0.0001	1.7 (1.8)	0.9 (1.4)	<0.0001
Triglycerides÷HDL cholesterol†	1.4 (2.1)	0.6 (1.6)	<0.0001	1.4 (2.0)	0.5 (1.6)	<0.0001
Non-HDL cholesterol	4.0 (1.2)	3.3 (1.0)	0.03	3.5 (1.0)	3.0 (0.8)	0.006
Diabetes mellitus (%)	33.3	1.2	0.004	43.8	5.6	<0.0001
RA characteristics						
Disease duration, years	16.7 (9.0)	14.4 (8.7)	0.5	13.6 (9.9)	12.6 (8.9)	0.9
Rheumatoid factor positive (%)	88.9	72.3	0.3	75.0	76.4	0.9
DAS28	4.5 (1.7)	3.4 (1.5)	0.05	4.4 (1.3)	4.1 (1.3)	0.1
Deformed joints†, n	3 (4)	3 (4)	0.8	5 (3)	6 (3)	0.6
Prednisone ever (%)	33.3	42.9	0.5	34.4	47.2	0.2
Current DMARD, n	1.6 (0.9)	2.2 (0.9)	0.06	2.6 (0.8)	2.5 (1.1)	0.9
Current methotrexate use (%)	55.6	81.0	0.06	90.6	93.1	1.0
Current chloroquine use (%)	22.2	48.8	0.1	75.0	79.1	0.7
Systemic inflammation						
ESR†, mm/hr	13 (3)	7 (3)	0.09	25 (3)	19 (3)	0.2
C-reactive protein†, mg/l	8.2 (3.1)	3.5 (3.4)	0.06	9.0 (3.6)	6.9 (2.8)	0.2
Other						
Education, years	12.7 (2.1)	12.8 (2.7)	0.8	8.3 (4.2)	7.1 (4.0)	0.6
AIMS depression†	4.1 (1.5)	2.8 (1.7)	0.04	3.4 (1.4)	3.3 (1.6)	0.7
Hypothyroidism‡ (%)	55.6	33.3	0.1	6.3	5.6	0.6
Hormone replacement therapy (%)	22.2	17.9	0.7	9.4	4.2	0.2

Results are expressed as mean (SD) unless indicated otherwise.
*p-value for comparisons between African black and Caucasian women after adjustment for age, sex and healthcare.
†Non-normally distributed variable for which geometric mean (SD) is given. ‡It includes subclinical and overt hypothyroidism and diagnosed when thyrotropin level was >4.94 mU/L or when thyroid hormone replacement therapy was used. RA: rheumatoid arthritis; MetS: metabolic syndrome; BMI: body mass index, DAS28: disease activity score in 28 joints, DMARD: disease modifying agents for rheumatic disease, ESR: erythrocyte sedimentation rate; AIMS: arthritis impact measurement scales; CIMT: common carotid artery intima-media thickness.

cular risk factors with plaque as well as the lack of associations of the respective risk factors, other than MetS blood pressure, with cIMT in African black women with RA, particularly in the face of an overall metabolic risk factor burden that was larger than in their Caucasian counterparts. Ultrasonographically determined carotid artery plaque is associated with a 10-year cardiovascular event rate risk of 39% in non-RA subjects (53) and reportedly predicts incident ACVD in patients with RA irrespective of population origin (40, 41). Taken together, our results indicate that metabolic risk factors in women with RA from developing groups of African descent do not as yet translate in severe atherosclerosis. Indeed, our findings are congruous with the distinctly low ACVD event rates (32-34, 38) despite the recent acquisition of more prevalent obesity, hypertension and diabetes in African black compared to Caucasian non-RA subjects (54). Furthermore, our data analysis indicates that the presence of RA does not alter the absence of metabolic risk factor related ACVD. Ultimately, metabolic risk may enhance atherogenesis in such persons, but only a longitudinal study will answer this question.

The burden of atherosclerosis was as large in African black compared to Caucasian women with RA in this study. Our results therefore indicate that rigorous systematic cardiovascular risk assessment should be performed irrespectively of metabolic risk factor profiles in African black women with RA.

Caucasian patients in the present investigation had a lower BMI and less

Table IV. Relationships of MetS characteristics with carotid artery intima-media thickness in African Caucasian and black women with RA.

	Caucasian women		Black women	
MetS characteristic	S β (95% CI)*	*p*-value	S β (95% CI)*	*p*-value
MetS waist	0.07 (-0.11–0.26)	0.4	-0.05 (-0.25–0.15)	0.6
MetS blood pressure	0.14 (-0.09–0.37)	0.2	0.20 (0.01–0.40)	0.04
MetS HDL cholesterol	0.11 (-0.08–0.28)	0.2	0.07 (-0.10–0.21)	0.4
MetS triglycerides	0.24 (0.05–0.39)	0.01	0.01 (-0.13–0.16)	0.9
MetS glucose	-0.01 (-0.19–0.11)	0.6	-0.10 (-0.23–0.06)	0.3
MetS definition	0.19 (0.01–0.35)	0.036	-0.08 (-0.24–0.08)	0.4
MetS criteria, n	0.21 (0.02–0.35)	0.028	0.04 (-0.10–0.20)	0.7

*Adjusted for age and healthcare centere. MetS: metabolic syndrome; S: standardised; β: regression coefficient; CI: confidence intervals; HDL: high-density lipoprotein.

Table V. Relationships of MetS characteristics with carotid artery plaque in African Caucasian and black women with RA.

	Caucasian women		Black women	
MetS characteristic	OR (95% CI)*	*p*-value	OR (95% CI)*	*p*-value
MetS waist	2.17 (0.79–5.93)	0.1	1.03 (0.94–1.12)	0.6
MetS blood pressure	1.19 (0.41–3.45)	0.7	1.60 (0.44–5.91)	0.5
MetS HDL cholesterol	2.91 (0.77–11.01)	0.1	0.44 (0.13–1.51)	0.2
MetS triglycerides	5.30 (0.99–28.46)	0.049	1.14 (0.36–3.59)	0.8
MetS glucose	1.93 (0.24–15.80)	0.5	1.12 (0.38–3.30)	0.8
MetS definition	4.74 (0.81–27.73)	0.08	0.58 (0.21–1.61)	0.3
MetS criteria, n	1.89 (1.09–3.26)	0.02	0.80 (0.53–1.23)	0.3

*Adjusted for age and healthcare centre. MetS: metabolic syndrome; OR: odds ratio; CI: confidence intervals; HDL: high-density lipoprotein.

frequent abdominal obesity and, consequently, a smaller MetS prevalence compared to those in published reports on metabolic risk in RA from the US (20, 24) and Europe (19, 21). Nevertheless, our results in Caucasians add to the available evidence that substantiates a role for metabolic risk in atherogenesis and cardiovascular risk assessment amongst patients with RA from developed populations (16-25). This includes the association of metabolic risk with systemic inflammation in that the DAS28 was, and the ESR and C-reactive protein concentrations tended to be higher in Caucasians with compared to those without the MetS in adjusted analysis. However, whereas systemic inflammation and disease activity explained the association between metabolic risk and coronary atherosclerosis in a study from the US by Chung *et al*. that included patients with both early- and long-standing RA (20), we found that the respective relationship was not materially altered by, and mostly independent of non-metabolic risk factors. This discrepancy is likely due to the fact that only patients with established treated RA were included in our study. Since lipid lowering agents decrease adverse cardiovascular outcomes, the fact that this intervention was more frequently employed in African Caucasian than in black women with RA further supports the presence of a relationship between MetS triglycerides and carotid atherosclerosis in the former but not the latter group.

Our study has further limitations. Our patients were exclusively women, the cross-sectional design of our investigation precludes drawing inferences on the direction of causality and the presence of less strong relationships between MetS characteristics and atherosclerosis than those found in our study may have eluded identification in view of our relatively small patient sample. Furthermore, we have recently reported that, compared to British Caucasians, non-RA black Africans experience much greater aortic reflective waves (54) and, therefore, possibly greater aortic blood pressure values for a given brachial blood pressure and, black Africans have reduced nocturnal blood pressure dipping that may produce target organ effects independently of conventional blood pressure (56). Consequently, central rather than brachial blood pressure evaluation and the use of ambulatory 24-hour day and night blood pressure recording may be required to adequately investigate the impact of the respective metabolic risk factor on atherogenesis in black Africans with RA.

Conclusion

In contrast to their African Caucasian counterparts, black women with RA experience a markedly increased metabolic risk factor burden that is however currently as yet not likely to be associated with atherosclerosis. The potential role of metabolic risk factors in atherogenesis in African black women with RA requires further assessment in longitudinal studies. Meanwhile, since the atherosclerosis extent was not reduced in African black compared to Caucasian women in the present study, our findings call for systematic cardiovascular risk management irrespective of metabolic risk factor profiles in African black women with RA.

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