Predictors of Arterial Stiffness in Connective Tissue Diseases: Insights from the Lupus Extended Autoimmune Phenotype (LEAP) Cohort Study

CRISTIANA SIEIRO SANTOS 1,2, Sarah Dyball 2 , Ellen Bruce 3 , I. N. Bruce 2,3 , B. Parker 2,3

1. Rheumatology Department, Complejo Asistencial Universitario de León (Spain); 2. The University of Manchester, Centre for Epidemiology Versus Arthritis, Manchester, United Kingdom; 3. Manchester University NHS FT, The Kellgren Centre of Rheumatology, Manchester, United Kingdom

Background

- Connective tissue diseases (CTDs), including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and Sjögren's disease (SjD), are associated with an increased risk of cardiovascular disease (CVD). Arterial stiffness, measured by carotid-femoral pulse wave velocity (cfPWV) and augmentation index (AIx), serves as a reliable marker of cardiovascular health and a predictor of adverse cardiovascular events.

- This study aimed to **assess arterial stiffness, measured by pulse wave velocity (PWV) and augmentation index (AIx), in individuals with CTDs including SLE, SSc, SjD, UCTD, MCTD, and/or overlap and IIM**, compared to healthy controls (HC) and to **identify factors associated with arterial stiffness** in this population.

Methods

- Participants from the Lupus Extended Autoimmune Phenotype (LEAP) cohort were enrolled in the study, which included patients with a diagnosis of a CTD and age- and gender-matched healthy controls. Sociodemographic data, CVD risk factors, and treatment details were collected for each participant. To identify independent associations with carotid-femoral pulse wave velocity (cfPWV) and brachial and aortic augmentation index (Aix), multivariate linear regression models were used.

Results

- We enrolled **382 CTD patients (167 with SLE, 75 with SjD, 53 with UCTD, 25 with SSc, 17 with overlap/MCTD, and 17 with myositis) and 28 healthy controls.** Median age was 51 ± 21 years old. 357 (93%) patients were female. SLE patients were prescribed immunosuppressive treatment, antimalarial and oral steroids treatment significantly more often ($p < 0.0001$) than those with other diagnoses.

- Patients with **SSc diagnosis had a higher cfPWV** compared with other CTDs ($\beta = 0.40$, $p = 0.04$). Across all CTDs, **increased cfPWV** was associated with **age** ($\beta = 0.04$, $p = 0.002$), **systolic blood pressure (SBP)** ($\beta = 0.01$, $p = 0.001$), **diastolic blood pressure (DBP)** ($\beta = 0.09$, $p = 0.002$), **and aortic AIx** ($\beta = 0.09$, $p < 0.0001$).

- **Aortic Aix** was associated with **male gender** ($\beta = 6.73$, $p < 0.0001$), **age** ($\beta = 0.32$, $p < 0.0001$), **DBP** ($\beta = 0.39$, $p = 0.01$) and **mean arterial pressure** (MAP) ($\beta = 0.73$, $p < 0.0001$). In addition, **AIx brachial** ($\beta = 0.08$, $p < 0.0001$), cfPWV ($\beta = 0.15$, $p = 0.03$), and **central blood pressure** ($\beta = 0.49$, $p < 0.0001$) were positively correlated with aortic AIx. Conversely, **heart rate** ($\beta = -0.44$, $p < 0.0001$) and **diastolic reflection area** ($\beta = -0.13$, $p < 0.0001$) showed significant negative associations. **Brachial AIx** was associated with **age** ($\beta = 0.46$, $p = 0.02$) as was a **diagnosis of SSc** was ($\beta = 12.67$, $p = 0.03$). Of note, **anti-Scl70 antibodies** across all CTDs had a negative association with brachial AIx ($\beta = -1.64$, $p = 0.08$).

Conclusions

- **Arterial stiffness** in patients with CTDs are particularly associated with **blood pressure parameters, heart rate, and a diagnosis of SSc diagnosis.** Our study underscores the complex interplay of traditional cardiovascular risk factors and disease-specific variables on cardiovascular health in CTDs and may inform targeted strategies for managing cardiovascular risk in this population.

Multivariate analysis

cfWV	**β**	**Sig**	**Lower 95% IC**	**Higher 95% CI**
Male gender	-0.83	0.13	-1.89	0.24
Age	**0.04**	**0.002**	**0.02**	**0.07**
SSc diagnosis	**0.40**	**0.04**	**0.04**	**2.62**
SLE diagnosis	0.31	0.37	-0.96	0.58
ACA	-0.48	0.48	-1.80	0.85
TG	0.17	0.26	-0.13	0.49
LDL	0.0002	0.80	-0.002	0.002
BMI	-0.001	0.54	-0.004	0.16
SBP	**0.01**	**0.001**	**0.004**	**0.16**
DBP	**0.09**	**0.002**	**0.03**	**0.33**
Central BP	-0.009	0.62	-0.04	0.03
Central pressure	-0.03	0.20	-0.08	0.02
Aix Brachial	0.005	0.91	-0.009	0.01
Aix aortic	**0.09**	**<0.0001**	**0.05**	**0.12**
Smoking	-0.009	0.95	-0.28	0.27
Non-white ethnicity	0.36	0.23	-0.23	0.94
Male gender	-0.87	0.13	-1.87	0.24

Aix aortic	**B**	Sig	Lower 95% IC	Higher 95% CI
Male gender	**6.73**	**<0.0001**	**3.35**	**10.12**
Age recruited	**0.32**	**<0.0001**	**0.23**	**0.40**
Oral steroid	0.29	0.76	-1.56	2.14
Low C4	1.91	0.07	-0.13	3.96
SBP	-0.006	0.92	-0.12	0.11
DBP	**0.39**	**0.01**	**0.96**	**0.69**
Hear rate	**-0.44**	**<0.0001**	**-0.58**	**-0.31**
MAP	**0.73**	**<0.0001**	**0.33**	**1.12**
Aix brachial	**0.08**	**<0.0001**	**0.05**	**0.11**
cfPWV	**0.15**	**0.03**	**0.02**	**0.29**
LVED	-0.04	0.14	-0.09	0.01
Central BP	**0.49**	**<0.0001**	**0.37**	**0.61**
Diastolic reflection	**-0.13**	**<0.0001**	**-0.20**	**-0.07**
Diastolic area	0.01	0.88	-0.15	0.17
Non-white ethnicity	1.10	0.65	-3.72	5.93
Aix brachial	**β**	Sig	Lower 95% IC	Higher 95% CI
Male gender	-2.72	0.72	-17.83	12.39
Age recruited	0.46	0.02	0.07	0.84
Antimalarials	**-4.22**	**0.03**	**-12.66**	**4.23**
Oral steroids	0.83	0.85	-7.91	9.57
Scl70	**-16.04**	**0.04**	**-33.80**	**1.71**
DBP	-0.57	0.38	-1.86	0.72
Heart rate	0.22	0.46	-0.37	0.82
MAP	0.35	0.70	-1.42	2.11
Aix aortic	**0.88**	**0.003**	**0.31**	**1.46**
CFPWV	0.41	0.67	-1.48	2.31
LVED	**0.03**	**0.76**	**-0.18**	**0.24**
Central BP	-0.07	0.99	-0.97	0.96
Central pulse pressure	-0.24	0.40	-0.81	0.32
Diastolic reflection	**-0.32**	**0.046**	**-0.64**	**-0.005**
SSc diagnosis	**12.67**	**0.03**	**6.49**	**31.82**

Cristiana Sieiro Santos
@cristianasieiro
cristysieirosantos@gmail.com

N.º 466