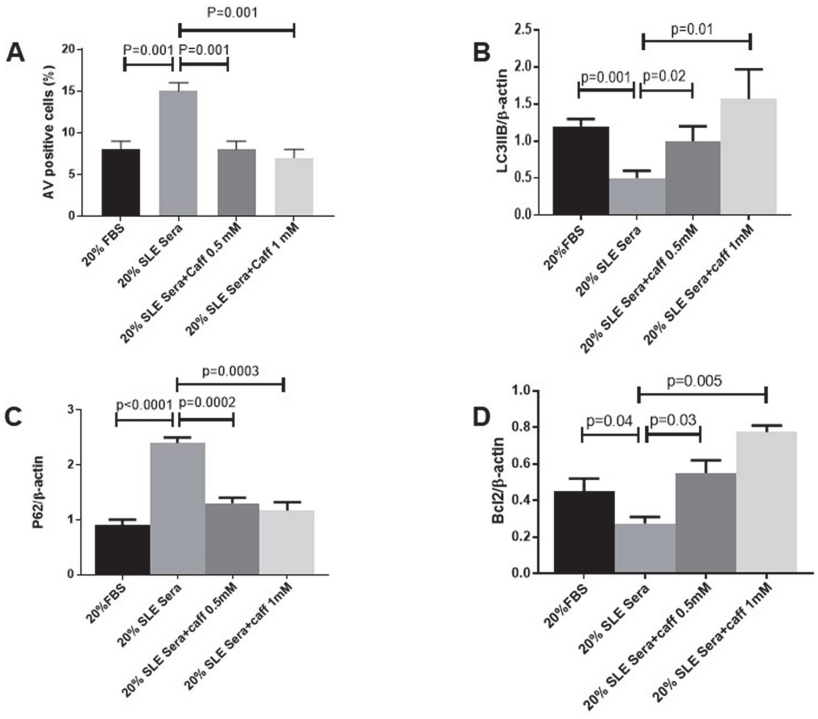

Abstract S03.1 Figure 1 Percentage of AV (A), LC311 (B), p62 (C), Bcl2 (D) positive cells in HD-EPCs cocultured with caffeine at 0.5 mM and 1 mM with and and without SLE sera

was to evaluate the role of caffeine intake on endothelial function in SLE patients, by assessing its effect on number and function of EPCs both ex vivo in SLE patients and in vitro in healthy donors (HD) treated with SLE sera.

Methods We performed a cross-sectional study enrolling SLE patients excluding patients with history of traditional cardiovascular risks factors. Caffeine intake was evaluated using a 7-day food frequency questionnaire. At the end of questionnaire filling circulating EPCs were detected by using a flow cytometry analysis. Subsequently, EPCs pooled from 6 HD were cocultured with caffeine at 0.5 mM and 1 mM with and without SLE sera. After 7 days, we evaluated the cells morphology and the ability to form colonies. Moreover, we analyzed for the percentage of annexin V-positive (AV) apoptotic cells by flow cytometry analysis and for levels of autophagy and apoptotic markers LC3-II, p62 and Bcl2 by western blot. Finally, EPCs were also treated with SLE sera, alone or in combination with caffeine at 1 mM, in the presence of protease lysosomal inhibitors E64d and Pepstatin A.

Results We enrolled 31 SLE patients (F:M 30:1, median age 43 years, IQR 18; median disease duration 144 months, IQR 180). We found a EPCs median percentage of 0.03% (IQR 0.04) observing a positive correlation between caffeine intake and EPCs percentage (p=0.03, r=0.4). Moving on in vitro experiments, HD EPCs treated with SLE sera and caffeine showed an improvement in morphology and in number of EPCs-CFU in comparison with those incubated with SLE sera without caffeine (p=0.0003). Moreover, the colonies treated with SLE sera were poorly organized in comparison with HD; the addition of caffeine restored the colony structure. After treated HD-EPCs with SLE sera we observed an increase in AV positive cells and p62 values and a reduction of LC3-II and Bcl2 values; the addition of caffeine was able to significantly reduce AV positive cells and p62 values and to significantly increased LC3-II and Bcl2 values (Figure 1A-D), without any significant differences between caffeine 0.5 mM and 1 mM treatment. Finally, in the presence of protease inhibitors, we didn't observe any significant difference in the autophagy and apoptotic markers values, compared to condition without inhibitors.

Conclusions Our data demonstrated the ability of caffeine in increasing the number of circulating EPCs in SLE patients. Moreover in vitro experiments seem to suggest a protective role of caffeine on EPCs survival and vitality through the promotion of autophagy and the inhibition of apoptosis.

REFERENCES

1. Westerweel *et al. Ann Rheum Dis* 2007.
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S03.2 PATTERNS OF RECURRENT THROMBOSIS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME –MULTICENTRE, REAL LIFE LONG TERM FOLLOW-UP

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10.1136/lupus-2022-elm2022.7

Background Antiphospholipid Syndrome (APS) is an acquired hypercoagulable condition associated with antiphospholipid antibodies (aPLs) presence. Data on re-thrombosis following APS-diagnosis is limited.

Methods Retrospective analysis of new thrombotic events among primary-APS (pAPS) patients followed for up to 15 years in three medical centres in Israel.

Results Among 312 primary-APS patients 143 (46%) had new thrombotic event classified to three patterns: (1) Arterial - associated with heart valve disease (OR 7.24, 95% C.I. 2.26–24.6), hypertension (OR 3, 95% C.I. 1.44–6.25), elevated anti B2-GPI IgM (OR 1.04, 95% C.I. 0.996–1.08), arterial thrombosis at presentation (OR 1.74 CI95% 0.992–3.26) and older age (41 vs. 34 years, p<0.001). (2) Venous – linked with venous thrombosis at presentation (OR 12.9, 95% C.I. 5.27–31.6, p<0.001), heart valve disease (OR 9.81 CI95% 1.82–52.9, p=0.018), aGAPSS (OR 1.15 CI95% 1.02–1.29) and younger age (31 vs. 36.5 years, p=0.001); (3) Combined pattern - associated with heart valve disease (OR 40.5 95% C.I. 7.7- 212) and pulmonary embolism (OR 7.47 95% C.I. 1.96–28.5).

A 4th variant 'the Breakthrough pattern' defined by re-thrombosis despite prophylactic therapy was observed in 100/143(70%) patients and linked with heart valve disease (OR 8. 95% C.I. 2.43–26.3), venous thrombosis at presentation (OR 2.61 95% C.I. 1.47–4.66), leg ulcers (OR 12.2, 95% C.I. 1.4–107), hypertension (OR 1.99, 95% C.I. 0.92–4.34) and higher aGAPSS (OR 1.08, 95% C.I. 0.99–1.18).

Conclusion In this real life observation, re-thrombosis was common among pAPS patients including in those recommended to receive prophylactic therapy. Different patterns of recurrence were identified and linked with presenting symptoms, specific serological markers, APS-manifestations and comorbidities. Studies that will address interventions to prevent recurrences of APS related events are needed.

S03.3 PATIENT-SPECIFIC AND DISEASE-RELATED DETERMINANTS FOR CARDIOVASCULAR DISEASE (CVD) RISK STRATIFICATION IN THE APPLE (ATHEROSCLEROSIS PREVENTION IN PAEDIATRIC LUPUS ERYTHEMATOSUS) CLINICAL TRIAL COHORT

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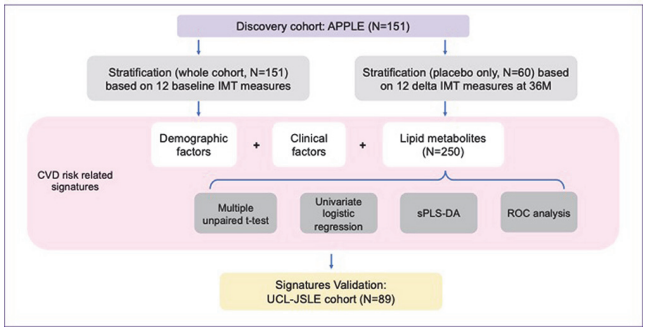
10.1136/lupus-2022-elm2022.8

Purpose The risk of developing CVD through atherosclerosis in juvenile-onset systemic lupus erythematosus (JSLE) patients is significantly increased. This study aimed to stratify and characterize JSLE patients at elevated CVD risk using patient/disease-related factors and metabolomic data from patients recruited to the APPLE (Atherosclerosis Prevention in Paediatric Lupus Erythematosus) clinical trial, designed to assess atherosclerosis development.

Methods Unsupervised hierarchical clustering was performed to stratify patients by arterial intima-media thickness (IMT) measurements at baseline (N=151) and carotid (c)IMT progression over 36 months (placebo arm only, N=60). Baseline metabolomic profiles (~250 serum metabolites) were compared between clusters using conventional statistics, univariate logistic regression, sparse Partial Least-Squares Discriminant Analysis (sPLS-DA) and random forest classifier. An independent cohort (UCL-JSLE cohort, N=89) with matching metabolomics, immunophenotyping and proteomics, was used to validate the discovered CVD risk-related signatures from the APPLE cohort.



Abstract S03.3 Figure 1

Results Baseline IMT stratification identified 3 clusters with high, intermediate, and low baseline IMT measurements and progression trajectories over 36 months, each having distinct racial/BMI/household education/income characteristics. Analysis of cIMT progression over 36 months identified 2 patient groups with high and low IMT progression. Unique metabolomic profiles differentiated high and low cIMT progression groups, with good discriminatory ability (0.81 AUC in ROC analysis) using the top 6 metabolites (Total cholesterol esters, Total cholesterol, Phospholipids in small LDL particles, Total cholesterol in small LDL particles, Free cholesterol in medium LDL particles and Total lipids in small LDL particles) selected from the analysis. cIMT progression over 36 months in the placebo group correlated positively with baseline disease activity (SLEDAI), damage score (SLICC), white blood cell count, serum complement C3, blood pressure (both systolic and diastolic) and BMI. Metabolomics signatures discovered from the APPLE cohort were applied to stratify JSLE patients in the validation cohort (UCL-JSLE), where 3 groups were identified with distinct metabolomics profiles indicating JSLE patients with high risk (N= 20), intermediate risk (N= 43) and low risk (N= 26) CVD-risk. Significant differences were observed in the frequency of classical monocytes (p=0.015) and nonclassical monocytes (p=0.005) when comparing high and low CVD risk groups in the UCL-JSLE cohort.

Conclusions Complex analysis of IMT patterns and progression in the APPLE trial cohort identified novel key determinants that could guide further research for CVD-risk stratification in JSLE.

Thursday 06 October 2022 from 17:30 to 19:00

S04 clinical challenges

S04.1 DISEASE ACTIVITY AND CLINICAL REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARISON BETWEEN PATIENT AND PHYSICIAN PERSPECTIVES BY MEANS OF PATIENT REPORTED OUTCOMES (PROS)

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10.1136/lupus-2022-elm2022.9