O26 FIRST INVESTIGATION OF THE PERFORMANCE OF VALIDATED CARDIOVASCULAR RISK SCORES IN A GLOBAL (UK/USA) COHORT OF CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH JUVENILE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2024-el.36

Objective Juvenile systemic lupus erythematosus (JSLE) is associated with increased cardiovascular disease (CVD)-risk from early in life. This is the first global (UK/US) JSLE study aiming to investigate the performance of CVD-risk scores.

Methods Patient data/CVD-risk factors/JSLE characteristics were collected from two JSLE cohorts: UK/UCL (N=109) and US/APPLE (**A**therosclerosis **P**revention in **P**ediatric **L**upus **E**rythematosus) trial (N=120) cohorts, stratified using cross-validated metabolomic signatures (*Nightingale*) of CIMT (carotid intima-media thickness) progression. QRISK3, Framingham (FRS), Atherosclerotic Cardiovascular Disease (ASCVD) and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) scores have been calculated/assessed for performance against robust CVD-risk stratification. We used descriptive statistics/correlation/ROC/linear regression analyses.

Results Mean patient age/disease duration for the UCL/APPLE cohorts were 26 ± 4.18 years/13.5± 4.71 years, and 15.60 ± 2.67 years/2.46± 2.44 years, respectively (P<0.001). QRISK3/FRS/ASCVD and PDAY scores classified 6.4%, 0%, 0% and 43.5% as high, and 1.8%, 0%, 1.6% and 21.8% as moderate risk, respectively, in the UCL cohort, while 22.4% and 48.5% were stratified as high and moderate risk, respectively using a validated CVD-risk metabolomic signatures. In the APPLE cohort only 1%, 0%, 0% and 3% patients were classified as high, and 2%, 0%, 4% and 10% as moderate risk by each of the scores above, despite CIMT (the best predictor of CVD) identifying 29.1% as high and 42.4% as moderate CVD-risk. PDAY-score had 60% sensitivity for high and 58% specificity for moderate risk stratification in the UCL cohort, while all the other scores failed to identify patients at risk. PDAY-score correlated with patients' age/disease duration/median SLEDAI/SLICC scores (r=0.78, 0.48, 0.28 and 0.3, respectively, P<0.05). Linear regression analysis found that age/disease activity were the strongest determinants of PDAY-score (one year increase in age/one point increase in median SLEDAI were associated with 1.13/0.41 points increase in PDAY-score, respectively, when sex/disease duration/damage/lipids/steroids were accounted for).

Conclusions CVD-risk scores, even if validated from age 14, do not adequately capture CVD-risk in JSLE. PDAY-score had moderate performance for young adults only, highlighting the need for better CVD-risk stratification tools in JSLE. Overall disease activity/patient age were the strongest predictors of PDAY-score but only in older JSLE patients.

Acknowledgements This work has been funded by grants from Lupus Research Alliance, USa and Versus Arthritis, UK.

O28 UNVEILING THE IMPACT OF NEUROPSYCHIATRIC INVOLVEMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS ON DAMAGE ACCRUAL

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10.1136/lupus-2024-el.37

Objective The link between neuropsychiatric involvement in systemic lupus erythematosus (NPSLE) and heightened morbidity, mortality, and organ damage, as well as detrimental impacts on health-related quality of life has been well-documented. However, the direct association between NPSLE and specific SLICC/ACR damage index (SDI) items, especially non-neuropsychiatric items, remains unclear. Herein, we sought to investigate the impact of NPSLE on organ damage accrual in a large lupus cohort.

Methods We conducted an analysis of baseline data derived from five phase III trials (BLISS-52, BLISS-76, BLISS-SC, BLISS-NEA, EMBRACE), encompassing a total of 3645 SLE participants. NPSLE involvement was defined as NP BILAG A/B/C/D or scores on any of the NP SLEDAI-2K domains (n=372); the non-NPSLE group comprised patients with NP BILAG E and no neuropsychiatric involvement based on the NP SLEDAI-2K domains (n=3273). We employed univariable logistic regression analysis in case of < 30 events, or multivariable analysis to adjust for age, disease duration, sex, and ethnic origin in all other cases.

Results The median/mean (IQR; SD) SDI score and SLE disease duration were 0; 0.62 (0–1; 1.09) and 4.51; 6.44 (1.56–9.32; 6.33) years, respectively. Compared with the non-NPSLE group, SLE patients with neuropsychiatric involvement had greater SDI scores (adjusted (a)OR: 2.70; 95% CI: 2.14–3.42; p< 0.001). This held true also after suppression of the NPSLE SDI items from the total SDI score ((a)1.54; 1.22–1.94; p< 0.001). As expected, neuropsychiatric involvement was associated with damage in the neuropsychiatric domain ((a)8.71; 6.64–11.44; p< 0.001). More importantly, neuropsychiatric involvement was associated with damage in the cardiovascular ((a)2.44; 1.61–3.69; p< 0.001), musculoskeletal ((a)1.76; 1.31–2.35; p< 0.001), and skin ((a)1.45; 1.00–2.11; p=0.05) domains. Dissecting the SDI domains into specific items, neuropsychiatric involvement was associated with established damage in terms of coronary artery disease ((a)2.88; 1.34–6.18; p=0.007), myocardial infraction ((a)2.90; 1.41–5.96; p=0.004), valvular disease (4.94; 1.65–14.81; p=0.004), muscle atrophy ((a)3.17; 2.05–4.92; p< 0.001), bowel infarction ((a)1.84; 1.11–3.04; p=0.018), and scarring alopecia ((a) 1.69; 1.12–2.56; p=0.013). Lastly, SLE patients with neuropsychiatric involvement were more likely to have developed premature gonadal failure ((a)1.97; 1.06–3.67; p=0.032) compared with SLE patients with no history of neuropsychiatric events.

Conclusions The intricate association between neuropsychiatric involvement in SLE and damage accrual extends beyond the realm of the nervous system, impacting the musculoskeletal, skin, and cardiovascular organ systems. Prospective research, especially survey in non-selected real-world SLE cohorts, would be required to determine the causal relationship between NPSLE and the various components of the