Results: Baseline data: mean age 39 years, 135 females, 18 men, histological class III, 53 cases, IV: 58 cases, pure V: 12 cases, III/IV + V: 30 cases. At 52w after biopsy, SLEDAI (16 → 2), BILAG (17 → 2) score is significantly decreased. Dose of PSL was reduced (48 → 9 mg). At 52w, all cases were classified as RR (125 cases, 82%) and NR (27 cases, 18%) by ACR/LUNAR remission criteria. Surprisingly, all cases of pure V reached remission. Class III or IV LN (RR 114 cases; 91% vs NR 27 cases; 100%, $p = 0.01$) and cellular/fibrocellular crescent formation (RR 51 cases; 40% vs NR 18 cases; 66% $p = 0.01$) were significantly higher in NR. Clinically, long disease duration ($p = 0.02$), coexisting hypertension (RR 7 cases; 6% vs NR 9; 33%, $p < 0.01$) and TMA (RR 1 case; 0.7%, NR 2 cases; 7%, $p = 0.02$), baseline urine protein (RR 1.5g vs NR 2.2g, $p < 0.01$), baseline low WBC ($p = 0.03$), baseline low IgG ($p = 0.02$) were detected. About therapeutic drugs, IVCY significantly improved remission rate (RR 84 cases 68% vs. NR 9 cases 41%, $p = 0.03$). After long-term observation, 52w NR was significantly lower eGFR level (RR 81 vs NR 50, $p < 0.01$, median observation period of 138 months). 3 cases developed ESRD and all of those cases show crescent formation.

Conclusion: As histological factors contributing to 52w-NR, class III or IV and crescent formation were detected. This result suggested that the therapeutic response was relatively better in cases with IC deposition lesions than those with inflammatory lesions. In LN, more-detailed pathological classification which could extract crescent formation might be required.

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FRI0247

PROGNOSTIC ROLE OF TUBULO-INTERSTITIAL INFILTRATE IN PATIENTS AFFECTED BY LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) occurs up to 50% of patients affected by Systemic Lupus Erythematosus (SLE) representing one of the major causes of morbidity and mortality in lupus population (1). Kidney biopsy is a fundamental tool for the diagnosis and management of lupus nephritis. The presence of pathological changes such as inflammatory infiltrate in glomeruli and/or in tubulo-interstitium are relevant in terms of prognosis and response to therapy (2).

Objectives: The aim of the study was to correlate the clinical and laboratory findings and the response to therapy with presence of glomerular and/or interstitial infiltrate in kidney section of patients with a biopsy-proven LN.

Methods: Kidney sections of patients with SLE undergoing a renal biopsy for diagnostically purpose were studied; samples were classified according to the 2004 International Society of Nephrology/Renal Pathology Society classification criteria (3). Clinical, laboratory and histological data were collected in a standardized, computerized and electronically filled form, including demographics, past medical history, autoantibody profile, previous and concomitant treatments. We assessed the disease activity by using SLEDAI-2K and remission in response to therapy was defined as the absence of renal impairment and as a score 0 of renal SLEDAI (proteinuria <500mg/24 hours, absence of hematuria and urinary casts) (4). All patients underwent to cyclophosphamide or mycophenolate treatment (5, 6). Two to three micron thick sections from paraffin-embedded blocks routinely stained with hematoxylin-eosin (HE) and Periodic acid-Schiff (PAS) for light microscopy investigation were re-evaluated. Predictive value of the presence of interstitial infiltrate on renal remission was evaluated. The results were expressed as mean±standard deviation (SD) depending on the distribution of the variables. The values of $P < 0.05$ were considered statistically significant.

Results: We evaluated 53 kidney samples from patients with LN (F:M = 51:2, mean age at biopsy 35±7.7 years; mean disease duration at date of biopsy 8±8.3 years). Class IV (46%) was the most common class

followed by class III (29%), class II (13%), class V (11.5%) and class VI (0.5%). Tubulo-interstitial infiltrate was found in 33 kidney specimens, with germinal centres (GC)-like features in 13 renal samples (Figure 1). During the follow up (6±3.8 years) the tubulo-interstitial infiltrate, either diffuse or with GC-like feature, was negatively correlated with renal remission ($P=0.03$).

Conclusion: Assessment and management of patients with LN are greatly facilitated by information obtained by renal biopsy. In the present study we demonstrate that the presence of tubulo-interstitial infiltrate is associated with a worse outcome in response to therapy. Our data highlight the importance of tubulo-interstitium damage, scarcely considered in the current classification criteria, since it represents a key point to predict long-term prognosis.

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Figure 1

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FRI0248

ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY IN PRIMARY SJÖGREN SYNDROME: A MARKER OF EROSIONS ON HIGH RESOLUTION ULTRASOUND OF HANDS AND WRISTS

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Background: Cyclic citrullinated peptides antibodies (anti-CCP) were described in primary Sjögren's syndrome (pSS). However, its possible associations with joint erosions, synovitis and tenosynovitis on high resolution ultrasonography of hands and wrists (US) in pSS are uncertain.

Objectives: To assess in pSS the US findings, and their possible associations with anti-CCP.

Methods: We have evaluated 97 consecutive pSS patients (2016 ACR/EULAR Classification Criteria), of both sexes, aged 18-76 years, and without meeting the 1987 ACR classification criteria for rheumatoid arthritis (RA). Twenty RA patients (disease duration <5 years, and without joint deformities), and 80 healthy controls with comparable mean age, gender and ethnicity were also included in a case-control study. Clinical evaluation was performed through a standardized protocol with interview and physical examination. Disease activity was measured according to EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). US was done in 36 joints and 36 tendon areas of wrists and hands, by the same rheumatologist with expertise in ultrasound, and blinded to autoantibody profile. Patients and controls also underwent X-ray of hands and wrists. Anti-CCP was determined by ELISA using a commercially available kit.

Results: Frequency of tenosynovitis on US was higher in the pSS group than in healthy controls (36.1 vs. 3.8%, $p < 0.001$). Moreover, the number of tenosynovitis was higher in the former group ($p < 0.001$). Importantly, the presence of erosions on US (27.8 vs. 7.5%, $p = 0.001$) and their number ($p = 0.005$) were greater in the pSS group than in healthy controls, with predominance of small erosions ($p = 0.015$). Comparative analysis between RA and pSS groups revealed that the frequency ($p < 0.001$) and number ($p < 0.001$) of synovitis on US were greater in the former group. The number of grade 1 synovitis was comparable between RA and pSS patients ($p = 0.354$). However, the number of grade 2/3 synovitis were higher in RA than in pSS patients ($p < 0.001$ / $p < 0.001$, respectively). Similarly, the number of erosions on US was higher in the RA group compared to pSS group ($p < 0.001$), particularly of moderate/large erosions

($p < 0.001$ / $p < 0.001$, respectively). ESSDAI had moderate correlation with the number of synovitis ($r = 0.302$, $p = 0.003$) and tenosynovitis ($r = 0.343$, $p = 0.001$) on US. In pSS patients, US detected 225% more erosions than X-ray. Anti-CCP was more frequent in RA patients (85%) than in pSS (16.5%) ($p < 0.001$). Anti-CCP was more frequent in pSS patients (16.5%) than in healthy controls (4.1%) ($p = 0.010$). In addition, this reactivity was associated with higher mean numbers of erosions in wrists ($p = 0.018$) and proximal interphalangeal joints ($p = 0.001$) on US in pSS patients.

Conclusion: US detected higher frequencies of tenosynovitis and erosions in pSS patients than in healthy controls, and the numbers of synovitis and tenosynovitis correlated with ESSDAI, suggesting that US is an important tool for the evaluation of these patients. Moreover, grade 2/3 synovitis and moderate/large erosions appear to be relevant for the distinction between pSS and RA. The additional observation that erosions are associated with anti-CCP in pSS seems to characterize a subgroup of patients with a severe underlying mechanism of joint damage. Grant from FAPESP: 2015/03756-4.

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FRI0249

THE RISK OF VENOUS THROMBOEMBOLIC EVENTS IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Although observational studies suggest people with systemic lupus erythematosus (SLE) have a heightened risk of venous thromboembolic events (VTE), meta-analyses that integrate evidence across studies to estimate the pooled risk have not been performed.

Objectives: To conduct a systematic review and meta-analysis to estimate the risk of VTE including pulmonary embolism (PE) and deep vein thrombosis (DVT) in patients with SLE.

Methods: We conducted a systematic review using MEDLINE and EMBASE from inception to March 2018 to identify observational studies (cohort and cross-sectional) that evaluated the risk of several major cardiovascular outcomes in patients with SLE compared to a general population or healthy controls (protocol published in PROSPERO 2018 CRD42018098690). Here we report the results for venous thromboembolic outcomes. Studies were included that provided effect estimates (relative risks or hazard ratios) for the calculation of pooled effect estimates. Random effects models were used to calculate pooled risk ratios (RR) and 95% confidence intervals (CI) separately for VTE, PE and DVT. Visualization of funnel plots and the Egger's test were used for evaluation of publication bias. The robustness of the results was tested using the leave one out function. Sensitivity analysis assessed the impact of removing high risk of bias studies (i.e. cross-sectional).

Results: A total of 9 studies were identified for inclusion into the meta-analysis; 7 for VTE (including two cross-sectional studies), 3 for DVT and 4 for PE. Meta-analysis of the VTE studies showed a significantly increased RR of 3.67 (95% CI: 2.10 to 6.42) for patients with SLE compared to a general population. Removing the two cross-sectional studies did not impact the results (RR 4.06 [95% CI: 3.12 to 5.28]). The pooled RRs for PE and DVT were 4.47 (95% CI: 1.79 to 11.15) and 5.51 (95% CI: 2.27 to 13.39), respectively. The statistical heterogeneity was high

with an I^2 ranging between 92% and 99%. Visual examination of the funnel plots showed evidence of publication bias, however this was not supported by the Egger's test. The leave one out function confirmed the robustness of the results.

Conclusion: Overall, the risk of VTE was found to be significantly higher, over three- to six-fold higher, among patients with SLE compared with the general population. Future research should focus on assessing the impact of traditional and SLE-specific modifiable risk factors on VTE to further identify SLE patients most at risk to support targeting prevention and treatment strategies.

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Abbreviations: RE, relative effects

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FRI0250

SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARABLE EFFECT OF TRADITIONAL CARDIOVASCULAR RISK FACTORS WITH RHEUMATOID ARTHRITIS

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Background: Both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients are associated with an increased and premature