subjected to flow cytometric analysis to determine the expression of amino acids-related markers.

Results: 1) Stimulation with the combination of BCR, IFN- α and TLR7/9 ligand induced PB differentiation accompanied by uptake of amino acids. PB differentiation was abrogated in the absence of essential amino acid methionine, and to a lesser extent leucine, but not in non-essential amino acid cystine. 2) LAT1 and CD98 are known amino acid transporters. Stimulation with BCR, IFN- α and TLR7/9 ligand induced CD98 expression but suppressed LAT1 expression. CD98 expression was higher in CD27^{hi}CD38^{hi} PB than in CD27^{hi}CD38^{lo} non-PB. 3) Previous studies reported that amino acids were perceived by the sensor, leading to mTORC1 phosphorylation. However, the mechanism by which amino acids activate other intracellular signaling pathways in B cells remains elusive. We found that methionine facilitated both the BCR and mTORC1 signals. In addition, the two signals synergistically induced EZH2 expression, which is well known as a transcriptional factor for histone modification via induction of H3K27me3, in the presence of methionine. 4) Methionine induced EZH2 expression, leading to suppression of BACH2, induction of BLIMP1, XBP1 and PB differentiation. These results indicate that EZH2 is a critical factor for PB differentiation in the presence of methionine. Assessment of the expression of amino acid transporters CD98, LAT1 and EZH2 in B cells in RA and SLE patients showed overexpression of CD98 and EZH2, but not LAT1, in SLE, compared with RA and control. In SLE patients, EZH2 expression level correlated with that of CD98 in B cells. EZH2 expression also correlated with ESR and disease activity scores, such as of SLEDAI and BILAG, in SLE patients.

Conclusion: The results indicate that essential amino acid methionine plays an important role in PB differentiation through the CD98-EZH2-axis. The pathological process of SLE seems to involve essential amino acids and their metabolic/activation pathways throughout the process of PB differentiation.

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SLE, Sjögren's and APS – clinical aspects (other than treatment)

THU0244 PULMONARY MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by inflammation and tissue damage mediated by the immune system. Respiratory manifestations are common in SLE, appearing in up to 50% of patients throughout their lives. Furthermore, it is associated with higher mortality.

Objectives: To describe the prevalence and characteristics of pulmonary involvement in patients with SLE

Methods: Observational, descriptive, cross-sectional, retrospective study performed in patients with SLE in follow-up by the Rheumatology Department of Valme Hospital. The following information is collected from medical records; age, sex, mean age at diagnosis, characteristics of pleuropulmonary involvement and ANA and antiDNA positivity.

Results: We studied 165 patients with SLE, with mean age of 37.01 $\pm$ 14.65 years, predominance of the female patients 153 (92.72%). Thirty eight of them had pulmonary involvement (23.03%), with a total of 47 episodes related to lung manifestations. Mean age at diagnosis was 39.70 $\pm$ 15.50 years. Below is shown information about lung involvement:

Variable	Prevalence	ANA +	antiDNA +	Hospitalization required
Pleuritis	19	18	5	17
Lupus pneumonitis	1	1	0	1
ILD	2	2	0	1

Shrinking lung	4	4	1	2
Pulmonary embolism	5	4	1	3
Other	16	15	9	10

Eleven patients (28.94%) presented pulmonary involvement at the time of diagnosis; pleuritis (10.63%) and only one case of interstitial lung disease, varicella pneumonia, shrinking lung syndrome, pulmonary embolism (PE) and bronchiolitis obliterans with organizing pneumonia. Two patients (4.24%) died due to severe respiratory failure secondary to bilateral pneumonia. Three of the 5 patients with PE were diagnosed with antiphospholipid syndrome secondary to SLE. Regarding treatment, most of patients who required hospitalization were in basic treatment with synthetic DMARDs (78.57% in monotherapy and 21.43% with double therapy) and only 2 patients with biologic DMARDs (Rituximab and etanercept). Six patients had no treatment because the pulmonary event was at time of diagnosis, 2 patients were with antiaggregating therapy and there was no information registered in two patients (episode before 1997). 91.10% of the patients presented positive for ANA, of which 37.14% (13 patients) also presented positive antiDNA. No information was collected about autoimmunity in one patient (2.12%).

Conclusion: Pulmonary involvement in SLE is prevalent, although a significant proportion may remain asymptomatic. The little prevalence of pulmonary manifestations in our series might be due to low mean age, according to the result of a recent systematic review where analysed more than 10000 patients and concluded pulmonary manifestations are more frequent in late-onset SLE. The differential diagnosis is broad and the infectious cause, the main cause of mortality in patients with SLE, must always be ruled out.

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THU0245 LOW SPECIFICITY OF THE PROPOSED 2017 ACR-EULAR CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COMPARED TO PREVIOUS CRITERIA IN SLE PATIENTS WITH NEUROPSYCHIATRIC SYMPTOMS

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Background: New ACR-EULAR SLE criteria have been proposed in order to attempt to improve classification for clinical and translational research (1, 2).

Objectives: We evaluated the performance of the proposed 2017 ACR-EULAR classification criteria in a cohort of SLE patients with neuropsychiatric (NP) symptoms and compared to previous classification criteria.

Methods: Medical records of patients visiting the NPSLE clinic of the Leiden University Medical Center (LUMC) between 2007-2017 were retrospectively evaluated. The performance of the proposed 2017 ACR-EULAR criteria, the 2012 SLICC criteria and the 1997 ACR criteria was evaluated by calculating sensitivity and specificity.

Results: 360 patients were included, of which 294 were clinically diagnosed with SLE. The newly proposed 2017 ACR-EULAR showed a sensitivity of 87% (95% CI: 83-91%) and a specificity of 74% (95% CI: 62-84%), as shown in Table 1. The 2012 SLICC criteria had a sensitivity of 85% (95% CI: 80-89%) and a specificity of 76% (95% CI: 64-85%). The 1997 ACR criteria had a sensitivity of 89% (95% CI: 85-92%) and a specificity of 89% (95% CI: 80-96%).

Sixty out of 294 patients fulfilled the proposed NP domain (delirium/psychosis/epilepsy). Using more specific criteria for NP symptoms related to SLE, as previously proposed by Bortoluzzi *et al.* (3), only 37 patients fulfilled this domain. However, this did not improve specificity, which remained 74% (95% CI: 62-84%).

In addition, the performance of the newly proposed criteria was evaluated including patients with more than 10 points, but negative ANA. This led to an increase of sensitivity to 90% (95% CI 86-94%), but also did not influence specificity.

Proposed 2017 ACR-EULAR classification criteria in SLE patients with NP symptoms			
	With adjusted NP domain	Including ANA negative patients	
Sensitivity (95% CI)	87% (83-91%)	87% (83-91%)	90% (86-94%)
Specificity (95% CI)	74% (62-84%)	74% (62-84%)	74% (62-84%)

Table 1. Performance of the proposed 2017 ACR-EULAR classification criteria for SLE

Conclusion: In a cohort of SLE patients with NP symptoms, the proposed 2017 ACR-EULAR classification criteria showed similar sensitivity as the 1997 ACR and the SLICC 2012 criteria, but lower specificity. Including ANA negative patients improved sensitivity.

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THU0246 ASYMPTOMATIC MYOCARDIAL DYSFUNCTION DETECTED BY SPECKLED TRACKING ECHOCARDIOGRAPHY (STE) IN ACTIVE SLE PATIENTS

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Background: Clinical myocarditis is seen in 10% of SLE patients, but autopsy studies have shown myocardial involvement in up to 50% of patients. Lupus myocarditis may be silent and can be detected by newer echocardiographic technique like STE especially when SLE is active.⁽¹⁾

Objectives: To study asymptomatic myocardial dysfunction by STE in active SLE patients.

Methods: All consecutive active SLE patients having a SLEDAI score ≥ 6 without any cardiac symptoms with disease duration ≤ 5 years aging between 18- 45 years, who attended the Rheumatology and Clinical Immunology department (Outpatient and Inpatient) of Medanta, The Medicity, Gurgaon, from May 2016 to March 2018, were enrolled. They were evaluated for myocardial dysfunction by using a novel ultrasound technique - STE, which was reviewed by one observer cardiologist. Global longitudinal systolic strain (GLSS) was calculated by STE in all patients. $GLSS < -19.7$ was considered as an indicator of myocardial dysfunction.⁽²⁾ Age and sex matched controls in the form of thirty healthy volunteer subjects were enrolled and their echocardiography findings were compared with active lupus patients. Atherosclerotic risk factors like hypertension, Diabetes Mellitus and age >45 years were excluded to avoid confounding effects.

Results: Fifty eight active lupus patients were analysed. In the cohort female: male ratio was 8.6:1, median duration of disease was 22 months (0.5 - 60) and mean SLEDAI was 11.02 ± 2.30 . GLSS was significantly low in active lupus patients compared to healthy controls ($p=0.0001$) suggestive of myocardial dysfunction.

In active lupus patients, abnormal echocardiographic findings (myocarditis, non-bacterial thromboendocarditis, pulmonary arterial hypertension and

pericarditis) were seen in 62.1%. Myocardial dysfunction was found in 27 (46.6%), 20 (34.5%) patients had low GLSS with normal left ventricular ejection fraction (LVEF) and these were significantly associated with APLA and anti Sm/RNP antibodies. Multivariate Logistic Regression analysis of myocardial dysfunction with SLEDAI and other system parameters showed that musculoskeletal, CNS, haematological and nephritis were associated with increased risk for developing higher disease activity and myocardial dysfunction, although it was not statistically significant.

Table 1. Comparison of GLSS and LVEF between active SLE patients and healthy control group patients

Table No.1 Comparison of GLSS and LVEF between active SLE patients and healthy control group patients

Echocardiographic parameters	Active SLE (n= 58)	Healthy control (n= 30)	P value
Mean LVEF, (Mean $\pm$ SD)	58 $\pm$ 7.5	61.7 $\pm$ 5	0.016*
Mean GLSS, (Mean $\pm$ SD)	-19.6 $\pm$ 3.0	-23.5 $\pm$ 3.2	0.0001*
PAH (>30 mmhg), n (%)	10(17.2 %)	0	-
NBTE, n (%)	10(18.2 %)	0	-
Pericarditis, n (%)	11(19.6 %)	0	-

Table No.2 Myocardial dysfunction in active SLE based GLSS < -19.7 %.

Parameters	No. of patients (n= 58)	%
GLSS < -19.7	27	46.6
$< LVEF 52\%$	7	12.1
Both low	7	12.1
GLSS < -19.7 with normal LVEF	20	34.5

Table 2. Myocardial dysfunction in active SLE based GLSS < -19.7 %.

Conclusion: Almost half of active lupus patients have silent myocarditis. GLSS is more sensitive in detecting asymptomatic myocardial dysfunction than LVEF. Regular Echocardiography with Speckled tracking should be performed in Lupus patients especially when disease is active.

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THU0247 LRRN4: A NOVEL PROGNOSTIC BIOMARKER OF RENAL OUTCOME IN LUPUS NEPHRITIS PATIENTS

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Background: Lupus nephritis (LN) is the most common organ-threatening manifestation of systemic lupus erythematosus (SLE) and can result in kidney deterioration and end-stage renal disease (ESRD). Newly discovered biomarkers exhibit qualities of disease activity and damage, predict long term preservation of renal function.

Objectives: Combine the transcriptomics profile of kidney with long-term renal outcome in LN patients, to explore the novel non-invasive predictive biomarker for renal outcome.

Methods: The transcriptomics profile of kidney in 24 LN patients was obtained by using Affymetrix human HTA 2.0 gene expression chip. Random Forest method was used to screen the candidate mRNA biomarkers by correlate the gene expression profile with eGFR slope during the follow-up (Mean time 5.2 ± 1.2 years). In addition, in an independent LN cohort enrolled 45 patients, qRT-PCR and immunochemistry staining was performed to validate the correlation of mRNA level and protein level of candidate gene with renal outcome.