Background: Antiphospholipid syndrome (APS) is a chronic autoimmune disease with significant morbidity and mortality. The recently developed damage index for APS (DIAPS) considers thrombotic APS specific damage.

Objectives: Herein we aimed to identify disease clusters based on clinical characteristics and compare DIAPS between these clusters in a single center cohort of patients with APS ± systemic lupus erythematosus (SLE).

Methods: This retrospective study included 237 consecutive patients with APS [114 primary APS (PAPS) and 123 SLE+APS]. Data regarding demographics, clinical and laboratory characteristics and cardiovascular risk factors were retrieved from the existing database and revised. Two-step cluster analysis was performed. Cumulative damage was calculated for all patients by applying DIAPS as described previously.

Results: 237 patients were classified into 4 subgroups by cluster analysis. Cluster 1 ($n=74$) consisted of older patients with arterial-predominant VT, livedo reticularis and increased cardiovascular risk, cluster 2 ($n=70$) of SLE+APS patients with thrombocytopenia and heart valve disease, cluster 3 ($n=59$) of patients with venous-predominant VT, less extra-criteria manifestations and cluster 4 ($n=34$) of patients with only PM with a lower frequency of extra-criteria features and cardiovascular risk (table 1).

Table 1. Demographic, clinical and laboratory characteristics of clusters

	All ($n=237$)	Cluster 1 ($n=74$)	Cluster 2 ($n=70$)	Cluster 3 ($n=59$)	Cluster 4 ($n=34$)	P
Age (years), median (range)	43 (20-81)	51 (20-81)	40 (27-72)	42 (24-69)	40.5 (26-65)	<0.001
Duration of disease (years), median (range)	9.5 (1-37.7)	13.1 (1-37.7)	10.4 (1-28.7)	8.5 (1-32.8)	7 (1-22.4)	0.028
Female, n (%)	198 (83.5)	56 (75.7)	61 (87.1)	47 (79.7)	34 (100)	<0.05
SLE, n (%)	123 (51.9)	31 (41.9)	46 (65.7)	32 (54.2)	14 (41.2)	<0.05
Vascular thrombosis, n (%)	191 (80.6)	73 (98.6)	59 (84.3)	59 (100)	0 (0)	<0.001
Arterial thrombosis, n (%)	109 (46)	50 (67.6)	31 (44.3)	28 (47.5)	0 (0)	<0.001
Venous thrombosis, n (%)	112 (47.3)	36 (48.6)	37 (52.9)	39 (66.1)	0 (0)	<0.001
Pregnancy morbidity, n (%)	117 (49.4)	22 (29.7)	46 (65.7)	15 (25.4)	34 (100)	<0.001
Livedo reticularis, n (%)	38 (16)	21 (28.4)	10 (14.3)	5 (8.5)	2 (5.9)	<0.01
Thrombocytopenia, n (%)	81 (34.2)	4 (5.4)	65 (92.9)	4 (6.8)	8 (23.5)	<0.001
Heart valve disease, n (%)	92 (38.8)	32 (43.2)	46 (65.7)	8 (13.6)	6 (17.6)	<0.001
Arterial hypertension, n (%)	101 (42.6)	49 (66.2)	34 (48.6)	18 (30.5)	0 (0)	<0.001
Hyperlipidemia, n (%)	103 (43.5)	69 (93.2)	26 (37.1)	0 (0)	8 (23.5)	<0.001
Smoking, n (%)	58 (24.5)	31 (41.9)	7 (10)	17 (28.8)	3 (8.8)	<0.001
Lupus anticoagulant, n (%)	156 (65.8)	53 (71.6)	48 (68.6)	35 (59.3)	20 (58.8)	0.36
Anticardiolipin IgG/IgM, n (%)	155 (65.4)	46 (62.2)	46 (65.7)	38 (64.4)	25 (73.5)	0.71
Anti-β2-glycoprotein I IgG/IgM, n (%)	93 (39.2)	25 (33.8)	33 (47.1)	26 (44.1)	9 (26.5)	0.13
Triple aPL positivity, n (%)	45 (19)	12 (16.2)	16 (22.9)	13 (22)	4 (11.8)	0.46

Cluster 2 had the highest cumulative damage (mean DIAPS 2.48 ± 1.67) followed by cluster 1 (2.24 ± 1.44), cluster 3 (1.69 ± 1.27) and cluster 4 (0.32 ± 0.68). Comparison of DIAPS (total and major domains) between the clusters is shown in figure 1.

Patients with SLE+APS had a higher mean DIAPS compared to those with PAPS (2.10 ± 1.61 vs 1.69 ± 1.47 , $P=0.046$). Cardiovascular domain was the most frequently affected DIAPS domain in both groups. Proteinuria and avascular necrosis were significantly more frequent in SLE+APS (9.8% vs 2.2%, $P=0.02$ and 5.7% vs 0%, $P=0.009$, respectively). DIAPS was positively correlated with disease duration ($r=0.192$, $P=0.003$).

Conclusion: Elder APS patients with arterial thrombosis and increased cardiovascular risk and SLE+APS patients with extra-criteria manifestations had higher cumulative DIAPS. Longer disease duration, higher frequency of major organ involvement and higher immunosuppressive usage may have contributed to this difference. Therefore, control of cardiovascular risk factors, prevention and effective treatment of SLE flares may help to reduce damage in these subgroups.

Figure 1. Comparison of mean DIAPS (total and major domains) between the clusters

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3260

POS0767

CLINICAL MANIFESTATIONS, TREATMENT, AND OUTCOMES OF "NON-CRITERIA" ANTIPHOSPHOLIPID SYNDROME IN COMPARISON WITH DEFINITE ANTIPHOSPHOLIPID SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Patients with laboratorial or clinical manifestations suggestive of antiphospholipid syndrome (APS) but not fulfilling the classification criteria [1] constitute a challenge in clinical practice.

Objectives: To establish a comparison between patients with "non-criteria" versus those with definite APS on the frequency of clinical manifestations, prescribed therapies and reported outcomes.

Methods: A systematic review of observational studies comparing "non-criteria" with definite APS patients was performed searching 4 electronic databases. Data was extracted on clinical manifestations, therapies and outcomes. Studies were analyzed globally and, where possible, grouped under four potential "non-criteria" APS subsets. Random-effects meta-analyses were performed.

Results: Fourteen studies were included, assessing a total of 3,238 participants (Table 1). In the meta-analysis, no difference was detected in the frequency of arterial events or thrombosis recurrence between "non-criteria" and definite APS. However, a lower frequency of venous events was observed in "non-criteria" patients (risk ratio [RR]=0.9; 95%CI 0.7-1.0; p-value=0.047, $I^2=0\%$; Q Cochran p-value=0.226). Regarding obstetric morbidity, no difference was observed in most outcomes, but previous history of intrauterine growth restriction was less frequent (RR=0.7; 95%CI=0.6-0.9; p-value=0.003, $I^2=0\%$; Q Cochran p-value=0.228) and the risk of prematurity in followed pregnancies lower in "non-criteria" patients. There was no significant difference in treatment frequency between groups, except for less use of hydroxychloroquine in "non-criteria" APS (RR=0.7; 95%CI=0.5-0.9; p-value=0.007, $I^2=46.5\%$; Q Cochran p-value=0.642). There was no significant difference in the risk of fetal loss between groups either with or without treatment (Figure 1). It should be noted that significant heterogeneity was observed in some outcomes across the studied categories. Most studies focused on "seronegative" and "incomplete laboratory" APS.

Table 1. Description of studies included in the systematic review.

Author, year (reference)	Number of Patients	
	Definite APS	NC-APS (global)
Mekinian, 2012 [2]	25	53
Rodriguez-Garcia, 2012 [3]	87	67
Conti, 2014 [4]	25	24
Ofer-Shiber, 2015 [5]	126	117
Mekinian, 2016 [6]	83	96
Omar, 2018 [7]	30	30
Signorelli, 2017 [8]	77	13
Fredi, 2018 [9]	85	81
Litvinova, 2018 [10]	41	17
Alijotas-Reig, 2019 [11]	1000	640
Ferreira, 2020 [12]	15	21
Liu, 2020 [13]	192	90
Li, 2020 [14]	34	94
Lo, 2020 [15]	12	24

Abbreviations – APS: Antiphospholipid Syndrome; NC-APS: Non-criteria antiphospholipid syndrome.

Conclusion: This review suggests an absence of marked differences in most of the evaluated variables regarding clinical manifestations, treatment and outcomes between "non-criteria" and definite APS. These results should be interpreted with caution in light of the low-quality evidence available and heterogeneity observed in some outcomes.

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A. Fetal loss without treatment

B. Fetal loss with treatment

C. Live births (irrespective of treatment)

Figure 1. Forest plot of studies included in the meta-analysis regarding pregnancy and treatment outcomes.

Acknowledgements: The authors wish to thank Helena Donato, from the Documentation Unit, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, for her assistance performing the search for the systematic review.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3353

POS0768

THE IMPACT OF ANTI-RO ANTIBODIES IN PREGNANT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREN'S SYNDROME

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Background: The presence of anti-Ro antibodies in female patients diagnosed with systemic lupus erythematosus (SLE) and primary Sjögren syndrome (SS) in their fertile years raises concern among the medical team due to the risk of neonatal lupus in their newborns (NB). (1)

Objectives: The aim of this study was to determine whether there are differences between the outcome of anti-Ro positive pregnancies in SLE and SS.

Methods: This is a retrospective observational study carried out in a Rheumatology tertiary center. We included anti-Ro positive female SLE and SS patients, who were diagnosed before or during pregnancy and followed in our clinic between 2003-2020. The diagnosis of SLE or SS was established according to the 2012 SLICC criteria and the 2016 EULAR/ACR criteria, respectively. Clinical, immunological and pregnancy parameters were recorded before (where available), during and after pregnancy, as well as maternal risk factors (smoking, BMI,

disease and medication history). Statistical analysis for continuous variables were performed with T-student test and categorical variables with Person Chi-square test, using IBM SPSS Statistics version 20.

Results: Eleven out of 65 anti-Ro positive SLE patients and 10 out of 153 anti-Ro-positive SS patients met the inclusion criteria and had 13 and 12 pregnancies, respectively. The mean age at diagnosis was 24.75 ± 5.19 years for SLE and 31.92 ± 4.05 years for SS, and the mean pregnancy age was 28.33 ± 4.05 years for SLE and 33.17 ± 3.63 years for SS. Nine (81.81%) SLE patients were diagnosed before pregnancy, while 6 (60%) of the SS patients were diagnosed during pregnancy. Two (18.18%) SLE and 1 (10%) SS were smokers, median BMI was 21 for both SLE and SS (1 SS patient was obese), 2 (18.18%) had a history of lupus nephritis, 6 (54.54%) LES patients had secondary antiphospholipid syndrome, out of which 1 had a previous miscarriage. In the SS group there were 3 previous miscarriages, one patient had a history of parotid lymphoma. The majority of both SLE and SS patients had moderate anti-Ro antibody titers (<200 U/ml) before as well as during pregnancy: 6 (46.5%) and 8 (61.53%) in SLE, 5 (41.6%) and 7 (58.3%) in SS. More preterm NB and stillbirths were encountered in SLE mothers, possibly due to the association of secondary antiphospholipid syndrome, both groups encountered 1 pregnancy loss, and cesarean delivery outweighed vaginal ones in both SLE and SS patients. (Table 1)

Table 1. Gestational age and delivery type according to maternal disease

Gestational age	SLE number (%)	SS number (%)
Full-term pregnancy	4 (30.76%)	10 (83.33%)
Late preterm births	4 (30.76%)	1 (8.33%)
Very preterm births	2 (15.38%)	0
Stillbirth	2 (15.38%)	0
Pregnancy loss	1 (7.69%)	1 (8.33%)
Delivery type		
Vaginal	3 (25%)	4 (36.36%)
Cesarean	9 (75%)	7 (63.63%)

Distribution of pregnancy outcome is exhibited in figure 1. There were 4 (33.33%) NB with cutaneous neonatal lupus all from SS mothers, 3 of whom used HCQ before and/or during pregnancy; and there were 5 NB with complete fetal atrioventricular block (AVB), 3 (25%) from SS mothers and 2 (15.38%) from SLE mothers. A history of HCQ usage was recorded in 3 out of these 5 mothers, and all 5 NB with complete fetal AVB were treated with dexamethasone, without success. Two NB died (both from SLE mothers) and 3 NB (all from SS mothers) needed pacemaker implantation. From the latter, 1 developed pacemaker cardiomyopathy and 1 developed sepsis.

Conclusion: Neonatal lupus seems to be more prevalent in anti-Ro positive SS patients than SLE patients, even though no difference was seen in anti-Ro titer between the two diseases. Fetal cardiac arrhythmia may lead to SS diagnosis. Dexamethasone did not improve the outcome of the fetal AVB.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.3378

POS0769

VALIDATION OF THE SIMPLE INDEX FOR DISEASE ACTIVITY OF SYSTEMIC LUPUS ERYTHEMATOSUS IN CHINESE PATIENTS

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