low-density lipoprotein cholesterol (LDL-C) levels. 22,1% had arterial hypertension (AH), 29,5% were current smokers, 27,4% had excess body weight, 3,1% had family history of cardiovascular diseases (CVD). Traditional risk factors for atherosclerosis were found in 80% out of 40 gender and age matching subjects from the control group, i.e., showing practically the same prevalence as in BD pts.

Table 1. The incidence-rate of traditional risk factors in BD patients and controls

Variables	BD pts (n=95)	Controls (n=40)	p
Age, years	29,0 [23,0;35,0]	29,0 [25,0;32,0]	NS
BMI, kg/m ²	23,1 [21,1;25,5]	23,8 [22,0;26,0]	NS
BMI ≥ 25 kg/m ² , n (%)	26 (27,4)	15 (37,5)	NS
Arterial hypertension, n (%)	21 (22,1)	4 (10)	NS
Family history of CVD	3 (3,1)	5 (12,5)	0,05
Cigarette smoking, n (%)	28 (29,5)	12 (30,0)	NS
Dyslipidemia, n (%)	73 (76,8)	27 (67,5)	NS
Total cholesterol, mmol/l	5,0 [4,3;6,1]	5,1 [4,5;5,7]	NS
Cholesterol > 5,0 mmol/l, n (%)	47 (49,5)	25 (62,5)	NS
TGs, mmol/l	0,92 [0,7;1,3]	0,89 [0,60;1,08]	NS
TGs > 1,7 mmol/l, n (%)	8 (8,4)	3 (7,5)	NS
LDL, mmol/l	3,36 [2,8;4,0]	3,3 [2,7;3,7]	NS
LDL > 3 mmol/l, n (%)	63 (66,3)	25 (62,5)	NS
HDL, mmol/l	1,19 [1,0;1,5]	1,35 [1,2;1,6]	0,06
HDL ≤ 1 mmol/l (male), ≤ 1,2 mmol/l (female) n (%)	30 (31,6)	5 (12,5)	0,03

Reduced HDL levels were more common in BD pts vs the controls - 30 (31,6%) vs 5 (12,5), $p=0,03$ as shown in table 1. Other traditional risk factors were similarly present in both groups with no significant difference between BD pts and the controls.

Analysis showed similar incidence of CV events (nonfatal myocardial infarction, angina pectoris and stroke) in both groups. There were no differences between BD pts and healthy people in terms of lifetime risk for CVD. High lifetime risk ≥ 20% was found in 4 BD pts vs 0 in the control group; moderate lifetime risk >10% < 20% - in 6,3% of BD pts vs 2,5% in the control group, and low lifetime risk < 10% - was found in 89,5% of BD pts vs 97,5% of the controls.

Average IMT values were significantly higher in BD pts - 0.68 [0.60;0.73] vs 0.63 [0.56;0.65], $p=0,008$, but at the same time, IMT thinning (up to < 0.5 mm) was significantly more common in BD pts - 32.6% vs 12.5% in the control group ($p=0,01$). HsCRP serum levels were significantly higher in BD pts (2.42 [0.5;8.8] mg / l) than in the control group (0.37 [0.15;0.75]), $p=0,001$. There was a correlation between hs-CRP and BMI in BD pts ($r=0,2$, $p<0,05$), but no correlation was found between hsCRP and BD activity/BD clinical manifestations.

Conclusion: Decreased HDL cholesterol levels were more common in BD patients than in the control group, just as thinning of IMT, most likely because of vasculitis.

Disclosure of Interests: None declared

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POS0116 HEART RATE VARIABILITY IN PATIENTS WITH BEHCETS DISEASE

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Background: Behcet's disease (BD) is a systemic vasculitis affecting all types and sizes of blood vessels. Heart rate variability (HRV) reflects sympathetic-parasympathetic imbalance in the autonomic NS regulation. Low HRV values are known as independent risk factor of death and non-fatal cardiovascular events in both - survivors of a myocardial infarction and in asymptomatic population.

Objectives: The aim of this study is to evaluate HRV in BD pts vs healthy controls.

Methods: The study group included 74 BD pts (53males/21females) with disease duration of 9,0 (5,0;15,0)/9,0 (7;20) years, and the control group - 32/15 age-matched healthy m/f. The following HRV parameters from 24h ECG ambulatory recording were assessed: MeanNN and time-domain variables, adjusted by MeanNN (SDNNn%, SDNNn%, RMSSDn%). Additionally, all traditional cardiovascular risk factors such as systolic blood pressure (SPB), smoking status, BMI values, dyslipidemia profile, ultrasonographic values of carotid intima-media thickness (IMT), and levels high sensitive CRP (hsCRP) as a marker of inflammation were evaluated.

Results: In BD patients HRV values (RMSSDn%) were significantly lower compared to healthy controls (table 1).

Table 1. HRV parameters in BD patients and control group

Parameters	Males		Females	
	BD (n=53)	Control (n=32)	BD (n=21)	Control (n=15)
Age, years	30 (24; 36)	30 (26; 35)	32 (26; 37)	28 (24; 31)
MeanNN, ms	810 (732; 849)	782 (732; 835)	776 (708; 830)	764 (694; 832)
SDNN n (%)	16,9 (13,6; 19,4)	17,2 (16,3; 21,1)	13,1 (11,3; 5,3)	12,2 (10,7; 14,6)
SDNNi n (%)	6,8 (5,1; 8,1)	6,8 (5,0; 8,3)	7,1 (6,1; 7,7)	5,2 (4,9; 5,7)
RMSSD n (%)	2,1 (1,5; 2,3)**	4,1 (2,7; 5,2)**	1,7 (1,4; 3,7)*	2,8 (2,2; 3,9)*

Data are presented in median values and interquartile range, * $p<0,05$, ** $p<0,005$ vs controls.

There was a significant negative correlation in BD patients between HRV (SDNNn%) and age ($r=-0,4$; $p=0,00$), disease duration ($r=-0,3$; $p=0,00$), BMI ($r=-0,2$; $p<0,01$), cholesterol levels ($r=-0,3$; $p=0,00$), LDLP ($r=-0,3$; $p=0,00$) and increased IMT ($r=-0,2$; $p=0,04$), and also between HRV (RMSSDn%) and age ($r=-0,2$; $p=0,04$), disease duration ($r=-0,2$; $p=0,01$), cholesterol levels ($r=-0,3$; $p=0,00$), HDLP ($r=-0,2$; $p=0,04$); a positive correlation was established between HRV (SNNNn%) and smoking ($r=-0,2$; $p=0,04$). The control group showed positive correlation between HRV (SNNNn%) and increased IMT ($r=0,4$; $p=0,01$).

Conclusion: HRV reduction reflects impaired sympathetic-parasympathetic regulation in BD pts, associated with pts' age, disease duration and presence of traditional cardiovascular risk factors: BMI, increased cholesterol levels, LDLP, and such asymptomatic manifestation of atherosclerosis as increased IMT.

Disclosure of Interests: None declared

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POS0117 RENAL AND OVERALL OUTCOMES OF DOUBLE-POSITIVE (ANCA AND ANTI-GBM ANTIBODIES) PATIENTS COMPARED TO ANCA-ASSOCIATED VASCULITIS PATIENTS WITH SEVERE RENAL INVOLVEMENT: A MULTICENTER RETROSPECTIVE STUDY WITH SYSTEMATIC RENAL PATHOLOGY ANALYSIS

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Background: Among small vessel vasculitis, double-positive patients (DPP), combining serum and/or histologic findings for glomerular basement membrane (GBM) disease, and anti-neutrophil cytoplasmic antibodies (ANCA), is a rare, newly and poorly described condition.

Objectives: We aimed to compare characteristics between DPP and ANCA-associated vasculitis patients (AAVP) with severe-renal-involvement.

Methods: Retrospective multicenter study comparing 33 DPP and 45 severe-renal-involvement (serum creatinine >300 µmol/L) AAVP, all with biopsy-proven nephropathy.

Results: Except for 2 patients (6%) who had pure renal presentation during their entire follow-up period, others exhibited at least one extrarenal manifestation: pulmonary involvement (64%), weight loss (39%), gastrointestinal involvement (33%), ENT manifestations (21%), musculoskeletal symptoms (21%), fever (18%), neurological (12%), cutaneous (6%) and/or cardiac (6%) signs. All DPP (including up to 18% exhibiting negative serum anti-GBM antibodies) presented severe acute kidney failure with histologic GBM involvement. Compared to our AAVP, they had higher serum creatinine (719 versus 501 µmol/L; $p=0,006$) and a higher of patients requiring initial renal replacement therapy (82% vs 36%; $p<0,001$). Berden classification significantly differed ($p=0,003$), with more crescentic glomerulonephritis and fewer sclerotic lesions in DPP. One-year renal survival was significantly lower in DPP than in AAVP (27% versus 64%; $p<0,0002$). With comparable proportions of ANCA subtypes (2/3 with anti-MPO autoantibodies),

numbers of extrarenal manifestations, remission-inducing immunosuppressants and median follow-ups (three years) between groups, relapse rates were similar: 9.1% of DPP and 10% of AAVP. Please, see the table 1 for more detailed data.

Conclusion: Although DPP have features of both kinds of eponymous vasculitis, the anti-GBM component is the dominant phenotype, with more severe renal presentation and prognosis compared to AAVP with severe renal failure. Simultaneous testing of both antibodies and a systematically performed renal biopsy should be recommended in all rapidly progressive glomerulonephritis patients to recognize this difficult-to-treat, rare disease.

Table 1. Comparison of clinical characteristics and outcomes between the cohorts of DPP and AAVP

	DPP n = 33	AAVP n = 45	p
Age (year)	71,5 [14 - 89]	63 [45 - 93]	0.14
Male	16 (48)	19 (42)	0.65
Birmingham Vasculitis Activity Score	18,1 ± 4,8	20,4 ± 5,4	0.07
Organ involvement (except kidney)	1,7 ± 0,8	1,9 ± 1,1	0.31
Serum creatinine (μmol/L)	719 [238 - 2412]	501 [310 - 1683]	0.006
ANCA (MPO/PR3)	22/11	34/11	0.45
Berden classification	n = 31	n = 44	0.003
s (sclerotic) / c (crescentic)	6 (19) / 22 (71)	12 (27) / 16 (37)	
f (focal) / m (mixed)	0 / 3 (10)	11 (25) / 5 (11)	
Brix renal risk score	n = 27	n = 44	0.000014
Low / Medium / High	0 (0) / 4 (15) / 23 (85)	1 (2) / 29 (66) / 14 (32)	
Initial immunosuppressive therapy			
IV Cyclophosphamide	25 (76)	40 (82)	0.14
Rituximab	1 (3)	3 (7)	0.64
Plasma exchanges	25 (76)	19 (42)	0.005
Maintenance treatment	17 (48)	40 (89)	0.046
Initial RRT requirement	27 (82)	16 (36)	0.00007
Renal recovery (% initial RRT requirement)	4 (12)	6 (38)	0.9
1 year renal survival	9 (27)	29 (64)	0.0002

Values are displayed as absolute number (%) or as median [range]. DPP: double positive patients; AAVP: ANCA associated vasculitis patients; MPO: myeloperoxidase; PR3: proteinase 3; RRT: renal replacement therapy; IV: intravenous.

Disclosure of Interests: None declared

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POS0118

A WORLDWIDE PHARMACOEPIDEMOLOGICAL UPDATE OF DRUG-ASSOCIATED ANCA-ASSOCIATED VASCULITIS AT THE TIME OF TARGETED THERAPIES

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Background: Several pharmacological classes are involved in drug-associated anti-neutrophil cytoplasmic antibody-associated vasculitis (DA-AAV). However, the literature data supporting the role a drug in the onset of DA-AAVs mainly rely on case reports or short series and implicate old treatments. Moreover, the advent of new treatments, including targeted therapies, may have modified the epidemiology of these adverse drug reactions (ADRs).

Objectives: To update this list by using a pharmacovigilance-based data mining approach.

Methods: We collected data on ADRs reported with the MedDRA preferred term "Anti-neutrophil cytoplasmic antibody positive vasculitis" up to November 2020, from the World Health Organization pharmacovigilance database. For each retrieved drug, a case/noncase analysis was performed, and disproportionate reporting was calculated by using the information component (IC). A positive IC025 value, which is the lower end of the 95% credibility interval, was considered significant.

Results: A total of 483 deduplicated individual case safety reports of DA-AAV involving 15 drugs with an IC025>0 were retrieved. DA-AAV occurred in 264 (71.2%, n=371) women, the median age at onset was 62 years [45-72], and the median time to onset between the introduction of the suspected drug and DA-AAV was 9 months [1-36]. DA-AAV occurrence was considered serious in 472 (97.7%, n=481) cases and fatal in 43 (8.9%) cases. The drugs associated with the highest disproportionate reporting were hydralazine, propylthiouracil, thiazole, sofosbuvir, minocycline, carbimazole, mirabegron, and nintedanib (Table 1).

Table 1. List of the 15 drugs associated with ANCA-associated vasculitis in the World Health Organization pharmacovigilance database with significant disproportional reporting, sorted by decreasing IC₀₂₅

Drug	N _{observed}	N _{fatal} (%)	IC ₀₂₅ / IC	ROR [95%CI]	Delay (in days) between the introduction of the drug and AAV, median [Q1-Q3] (n available)
Hydralazine	208	19 (9%)	8.2 / 8.4	2683.5 [2269.3-3173.3]	1277 (n=1)
Propylthiouracil	108	4 (4%)	7.2 / 7.5	1201.5 [974.8-1480.9]	1003 [425-1959] (n=19)
Thiamazole	40	5 (13%)	5.2 / 5.6	138.7 [100.7-191.1]	411 [58-966] (n=6)
Sofosbuvir	46	0	4.9 / 5.3	74.6 [55.3-100.8]	(n=0)
Minocycline	17	0	3.8 / 4.6	72.4 [44.7-117.3]	(n=0)
Carbamazole	6	0	2.0 / 3.4	44.9 [20.1-100.4]	92 (n=1)
Mirabegron	7	2 (29%)	1.5 / 2.7	11.1 [5.3-23.3]	291 [289-415] (n=3)
Nintedanib	6	2 (33%)	1.4 / 2.8	14.2 [6.3-31.7]	56 [36-132] (n=4)
Penicillamine	4	1 (25%)	1.4 / 3.1	170.3 [63.5-456.3]	(n=0)
Influenza vaccine	29	2 (7%)	1.3 / 1.9	4.1 [2.8-6.0]	24 [20-26] (n=7)
Allopurinol	7	2 (29%)	1.2 / 2.4	8.0 [3.8-16.8]	(n=0)
Rifampicin	7	2 (29%)	0.6 / 1.9	4.7 [2.2-9.8]	(n=0)
Peginterferon alfa-2b	4	0	0.3 / 2.1	7.0 [2.6-18.6]	98 (n=1)
Montelukast	4	4 (100%)	0.2 / 1.9	5.8 [2.2-15.5]	(n=0)
Rosuvastatin	6	0	0.1 / 1.5	3.4 [1.5-7.5]	(n=0)

IC: information component; ROR: reporting odds ratio; CI: confidence interval; AAV: ANCA-associated vasculitis

Conclusion: This study strengthens the previously suspected association but also identifies 3 new drugs that may cause DA-AAV. Particular attention should be given to these drugs by prescribers and in experimental studies.

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POS0119

RENAL INVOLVEMENT AND NEED OF RENAL REPLACEMENT THERAPY IN ANCA ASSOCIATED VASCULITIS IN A SPANISH SINGLE-CENTER STUDY

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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EPGA). Renal involvement is frequent in AAV and is an important factor for morbidity and mortality.

Objectives: The main objective of this study was to analyze the demographic, clinical, histological and therapeutic characteristics of renal involvement in patients with AAV and the risk of renal replacement therapy (RRT) or death.

Methods: Retrospective observational study of 56 patients with AAV fulfilling classificatory criteria and renal involvement diagnosed between 1995 and 2020 from a Spanish tertiary centre. We studied the histological involvement (according to the 2010 classification in focal, crescentic, mixed or sclerotic), immunofluorescence (IF) and the treatment received with the risk of RRT or death.

Results: We included 56 patients diagnosed with AAV and renal involvement. The mean age was 61.08±4.05 years; 58.9% were women. The mean follow-up