

Supplemental data

Diagnosis	Bad Bramstedt	Copenhagen	Leuven	Maastricht	Total
Controls	189	237	246	252	924
GPA	40	38	40	68	186
MPA	26	8	15	16	65
Total	255	283	301	336	1175

Supplementary data Table S1. Distribution of controls, GPA and MPA across the centers.

ENT	Lung	kidney	Nervous system	Bad Bramstedt		Copenhagen		Leuven		Maastricht	
				GPA	MPA	GPA	MPA	GPA	MPA	GPA	MPA
			X	4	3			1	1	1	3
X				15	3	17		9		12	
X			X	2						1	
	X			4	5			1	1	1	2
	X		X	1	1			1	1	1	1
X	X			8		7		5		4	
X	X		X	1		2		1		1	
		X			4	8	6	3	1	16	9
		X	X		1			2		3	
X		X				1	2	4	1	2	
X		X	X					1		1	
	X	X			3			4	3	2	1
	X	X	X		3			4	4	1	
X	X	X		1		3		8	1	15	
X	X	X	X	4				1		4	

Supplementary data Table S2. Distribution of organ involvement in AAV patients. The table shows the number of GPA and MPA patients with ENT, lung, kidney or nervous system involvement and combinations thereof. The data are shown for each participating center. In AAV patients, there was involvement of ENT, lung, kidney and the nervous system in, respectively, 49%, 42%, 54% and 20% of the patients.

	Bad Bramstedt	Copenhagen	Leuven	Maastricht
Drug-induced vasculitis			1	
Organ-specific autoimmune disease		5	4	4
Inflammatory disease		86	15	81
Allergic disease		4	1	
Infectious disease		31	17	30
Malignant disease		10	10	11
Chronic fatigue syndrome			46	
Miscellaneous		72	90	75
Systemic autoimmune disease				
✓ <i>SLE</i>	59	7	16	1
✓ <i>Sjögren's syndrome</i>	30	2	8	1
✓ <i>Systemic sclerosis</i>	11	3	4	1
✓ <i>MCTD</i>		2	3	
✓ <i>Inflammatory myopathy</i>			1	
✓ <i>Rheumatoid arthritis</i>	89	5	6	6
✓ <i>Rheumatoid vasculitis</i>		2		
✓ <i>Still's disease</i>		3		
✓ <i>UCTD</i>			8	1
✓ <i>Antiphospholipid syndrome</i>		1		2
✓ <i>RS3PE, Sweet, Cogan syndrome</i>			3	
✓ <i>PAN</i>		1	9	1
✓ <i>PMR</i>			3	1
✓ <i>Psoriatic arthritis</i>			1	2
✓ <i>Takayasu arthritis</i>		1		
✓ <i>Arteritis temporalis</i>		1		
✓ <i>Cryoglobulinemia</i>				1
✓ <i>Cutaneous lupus</i>				1
✓ <i>Bechterew</i>				1

Supplementary data Table S3. Distribution of medical conditions in the control population.

MCTD: mixed connective tissue disease; PAN: polyarteritis nodosa; PMR: polymyalgia rheumatic; SLE: systemic lupus erythematosus; RS3PE: remitting seronegative symmetrical synovitis with pitting oedema.

Test	AUC	95% CI
1	0,910	0,879 to 0,942
2	0,900	0,867 to 0,933
3	0,878	0,838 to 0,917
4	0,890	0,859 to 0,921
5	0,891	0,856 to 0,926
6	0,902	0,869 to 0,936
7	0,905	0,872 to 0,937
8	0,888	0,851 to 0,925
9	0,814	0,779 to 0,849
10	0,882	0,851 to 0,912

Supplementary data Table S4

Area under the curve (AUC) for eight antigen-specific immuno-assays for PR3-ANCA [1-8] and two indirect immunofluorescence (IIF) methods for C-ANCA performed at two sites [Copenhagen (9) and Bad Bramstedt (10)] in 186 GPA patients and 924 controls.

The immuno-assays included were from Inova [QuantaLite (1) and QuantaFlash (2)], Thermo-Fisher (EliA) (3), Bio-Rad (BioPlex 2200) (4), Euro-Diagnostica (5), Orgentec (6), Euroimmun (7), and Medipan (CytoBead assay) (8).

Test	AUC	95% CI
1	0,953	0,919 to 0,986
2	0,935	0,894 to 0,976
3	0,934	0,888 to 0,980
4	0,937	0,897 to 0,977
5	0,936	0,888 to 0,983
6	0,931	0,883 to 0,980
7	0,943	0,900 to 0,985
8	0,870	0,808 to 0,932
9	0,900	0,856 to 0,943
10	0,908	0,863 to 0,953

Supplementary data Table S5

Area under the curve (AUC) for eight antigen-specific immuno-assays for MPO-ANCA [1-8] and two indirect immunofluorescence (IIF) methods for P-ANCA performed at two sites [Copenhagen (9) and Bad Bramstedt (10)] in 66 MPA patients and 936 controls.

The immuno-assays included were from Inova [QuantaLite (1) and QuantaFlash (2)], Thermo-Fisher (EliA) (3), Bio-Rad (BioPlex 2200) (4), Euro-Diagnostica (5), Orgentec (6), Euroimmun (7), and Medipan (CytoBead assay) (8).

AUC for Cytobead MPO-ANCA was significantly lower than AUC of all other immuno-assays for MPO-ANCA.

Euroimmun immuno-assay		Orgentec immuno-assay		Controls	GPA	MPA
PR3-ANCA	MPO-ANCA	PR3-ANCA	MPO-ANCA			
neg	neg	neg	neg	886	21	5
neg	neg	neg	pos	3	0	1
neg	neg	pos	neg	5	0	0
neg	pos	neg	neg	4	2	4
neg	pos	neg	pos	15	18	51
neg	pos	pos	pos	0	0	1
pos	Neg	neg	neg	6	0	0
pos	Neg	neg	pos	0	1	0
pos	Neg	pos	neg	1	143	3
pos	Neg	pos	pos		1	
pos	Pos	neg	neg	1		
pos	Pos	neg	pos	1		
pos	Pos	pos	pos	2		
				924	186	65

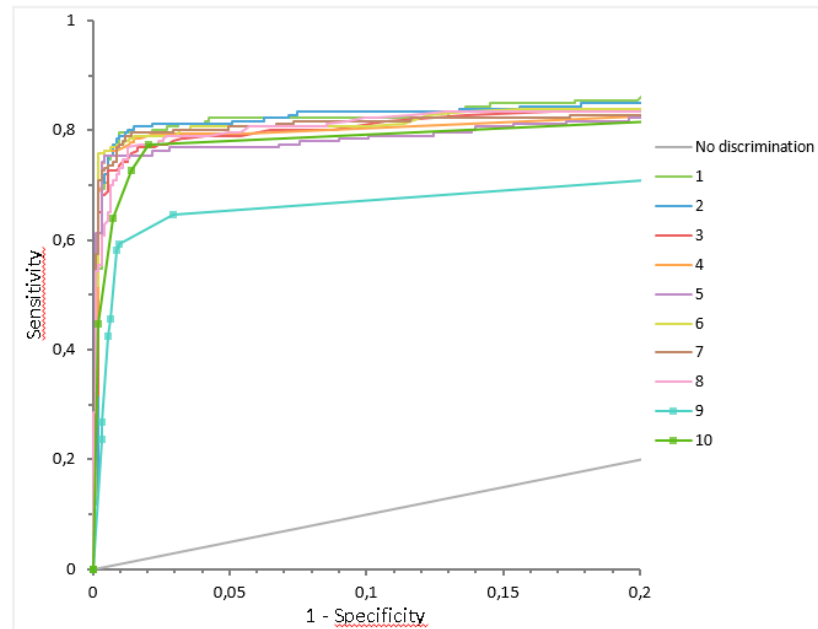
Supplementary data Table S6. Comparison between results obtained by two immuno-assays.

Although the concordance between the different antigen-specific immuno-assays is high, it is not absolute. An example of the comparison between two assays (Euroimmun and Orgentec) is illustrated in Supplementary data Table S4. Assays from Orgentec detected MPO-ANCA in 1/66 MPA patients that were not detected by assays from Euroimmun, whereas assays from Euroimmun detected MPO-ANCA in 2/193 GPA patients and in 4/66 MPA patients that were not detected by assays from Orgentec.

Besides, assays from Euroimmun detected PR3-ANCA in 6/936 controls and MPO-ANCA in 4/936 controls that were not detected by assays from Orgentec, whereas assays from Orgentec detected PR3-ANCA in 5/936 controls and MPO-ANCA in 3/936 controls that were not detected by assays from Euroimmun.

Supplementary Figures

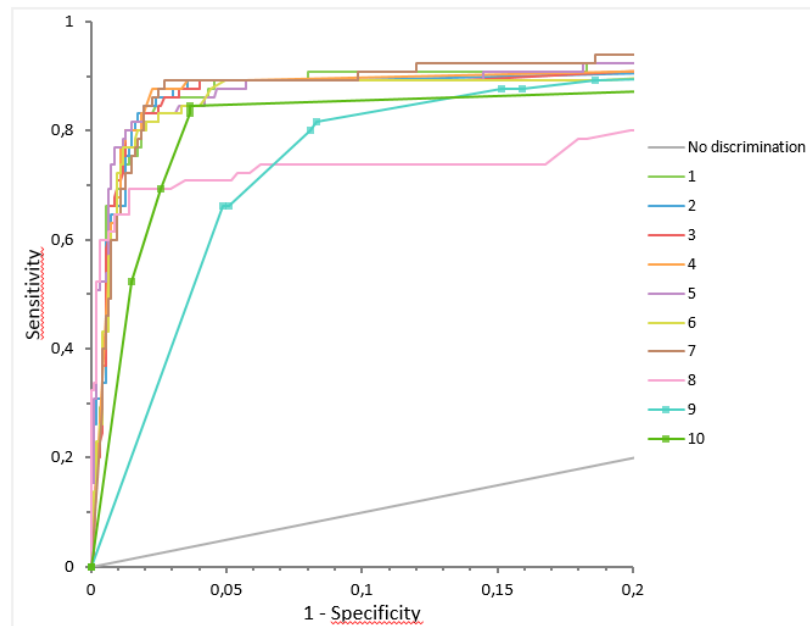
Supplemental Data - Figure S1. C-ANCA and PR3-ANCA in GPA (n=186) and controls (n=924).



Area under the curve (AUC) for eight antigen-specific immuno-assays for PR3-ANCA [1-8] and two indirect immunofluorescence (IIF) methods for C-ANCA performed at two sites [Copenhagen (9) and Bad Bramstedt (10)] in 193 GPA patients and 936 controls.

The immuno-assays included were from Inova [QuantaLite (1) and QuantaFlash (2)], Thermo-Fisher (EliA) (3), Bio-Rad (BioPlex 2200) (4), Euro-Diagnostica (5), Orgentec (6), Euroimmun (7), and Medipan (CytoBead assay) (8).

Supplemental Data - [Figure S2](#). P-ANCA and MPO-ANCA in MPA (n=65) and [controls](#) (n=924)



Area under the curve (AUC) for eight antigen-specific immuno-assays for MPO-ANCA [1-8] and two indirect immunofluorescence (IIF) methods for P-ANCA performed at two sites [Copenhagen (9) and [Bad Bramstedt](#) (10)] in 66 MPA patients and 936 controls.

The immuno-assays included were from [Inova](#) [[QuantaLite](#) (1) and [QuantaFlash](#) (2)], [Thermo-Fisher](#) ([EliA](#)) (3), [Bio-Rad](#) ([BioPlex 2200](#)) (4), [Euro-Diagnostica](#) (5), [Orgentec](#) (6), [Euroimmun](#) (7), and [Medipan](#) ([CytoBead assay](#)) (8).