

## Supplementary Material:

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**Supplementary Table S1:** Risk of bias of included studies on the Newcastle-Ottawa scale

Study		Year of Publication	Selection (Up to 4)	Comparability (Up to 2)	Outcome (Up to 3)	Total
1	Córdova-Sánchez <i>et al.</i> (8)	2016	3	1	2	6
2	Villacorta <i>et al.</i> (20)	2016	4	2	3	9
3	Shah <i>et al.</i> (17)	2015	4	1	3	8
4	Chen <i>et al.</i> (5)	2007	3	1	3	7
5	Eisenberger <i>et al.</i> (18)	2005	2	2	2	6
6	Lee <i>et al.</i> (7)	2015	4	2	3	9
7	Kantauskaite <i>et al.</i> (33)	2018	4	2	3	9
8	Shah <i>et al.</i> (19)	2015	3	1	2	6
9	Iwakiri <i>et al.</i> (34)	2013	4	1	3	8
10	Hung <i>et al.</i> (6)	2006	4	2	3	9
11	Hedger <i>et al.</i> (4)	2000	4	2	3	9
12	Sokolowska <i>et al.</i> (35)	2014	4	1	3	8
13	Sharma <i>et al.</i> (36)	2016	3	1	2	6

**Supplementary Table S2:** Systematic review of publications comparing clinical presentation, histopathological findings, outcomes in ANCA negative versus positive patients.

Author	Year	Location	Study design	ANCA negative (n)	Sex Male (%)	Age Years, (mean $\pm$ SD)	eGFR ml/min, (mean $\pm$ SD)	RRT n (%)	Clinical Presentation	Histopathology		Outcomes			
										Berden Classification	Histology Findings	ESKD	Relapse	Mortality	
1	Córdova-Sánchez <i>et al.</i> (8)	2016	Mexico City	Single Centre, retrospective	6	2 (33)	48.5 $\pm$ 19	20.3 $\pm$ 16	2 (33.3)	100% kidney involvement. 83.3% presented with RPGN	1 Focal 2 Sclerosed	-	-	-	50% mortality at EOS
2	Villacorta <i>et al.</i> (20)	2016	Spain	Multicentre, retrospective	29	20 (69)	54.8 $\pm$ 17.2	24.9 $\pm$ 21.5	10 (34.4)	Similar extra renal manifestation	Crescentic class most common	Higher % of mesangial proliferation & less tubulitis	No significant difference	No significant difference	No significant difference
3	Shah <i>et al.</i> (17)	2015	USA	Single Centre, retrospective	17	9 (53)	-	16.6 $\pm$ 10.25	8 (47.1)	Less paranasal involvement. kidney function worse at presentation	-	Higher degree of interstitial fibrosis	41% developed ESKD	Shorter time to remission	1-year survival similar
4	Chen <i>et al.</i> (5)	2007	China	Single Centre, retrospective	28	16 (57)	39.7 $\pm$ 17.0	-	15 (53.6)	Less extrarenal involvement	-	Lower % of normal glomeruli	Worse renal survival	-	25% mortality at EOS
5	Eisenberger <i>et al.</i> (18)	2005	Europe	Multicentre, retrospective	20	15 (75)	61.3 $\pm$ 13.1	-	4 (20)	High prevalence of constitutional symptoms and joint involvement	-	Moderate to severe interstitial infiltrates. 50% crescents, 21% sclerotic.	-	-	35% over 5 years
6	Lee <i>et al.</i> (7)	2015	Korea	Single Centre, retrospective	6	6 (100)	67.5 $\pm$ 7.7	25.2 $\pm$ 17.8	-	-	-	60% had severe interstitial inflammation 9.8% global sclerosis and 52.6% crescents	The HR of ESKD was 3.190 times in ANCA -VE patients.	-	33% mortality at EOS

7	Kantauskaite <i>et al.</i> (33)	2018	Lithuania	Single centre, retrospective	32	-	-	-	-	-	Focal: 48% Crescentic: 37.5% Sclerotic: 25% Mixed: 33.3%	-	No significant difference	-	No significant difference
8	Shah <i>et al.</i> (19)	2015	USA, Europe	Multicentre, retrospective	2	1 (50)	64.5 ± 4.95	13.5 ± 9.2	1 (50)	-	Sclerotic: 50% Mixed: 50%	-	-	1 relapse at 24 months	One patient died at EOS
9	Iwakiri <i>et al.</i> (34)	2013	Japan	Multicentre, retrospective	11	-	-	-	6 (54.5)	-	Focal: 27.3% Crescentic: 36.4% Sclerotic: 9% Mixed: 27.3 %	-	-	-	-
10	Hung <i>et al.</i> (6)	2006	Taiwan	Single centre, retrospective	15	8 (53)	45.1 ±13.5	-	4 (26.7)	26.7% pulmonary renal syndrome. 73.3 % renal limited disease	-	Less crescents, more chronic glomerular lesions	Worse renal survival	-	-
11	Hedger <i>et al.</i> (4)	2000	UK	Population based, retrospective	35	17 (49)	61 ±15	-	19 (54.3)	Shorter prodrome and less systemic involvement	-	Crescents seen in 48% of glomeruli	-	-	-
12	Sokolowska <i>et al.</i> (35)	2014	Poland	Single centre, retrospective & prospective	35	10 (29)	40 ±13.4	-	-	Less kidney and skin involvement	-	-	-	No significant difference	One patient died at EOS
13	Sharma <i>et al.</i> (36)	2016	India	Single centre, retrospective	33	18 (55)	35.4 ±13.5	16.1 ±3.78	19 (57.6)	Renal limited with lower rates of extra renal symptoms	Focal: 9.1% Crescentic: 66.7% Sclerotic: 12.1% Mixed: 12.1 %	Higher % of cellular crescents and interstitial fibrosis	68.4% ESKD	-	22.2% mortality
14	Floyd <i>et al.</i>	2021	UK	Single centre, retrospective	32	21 (66)	51.4 ±19.7	15.7 ±14.7	19 (59.3)	Renal limited with lower rates of extra renal symptoms	Focal: 37.5% Crescentic: 15.6% Sclerotic: 12.5% Mixed: 34.4%	Lower % of normal glomeruli	More progressed to ESKD	Lower relapse rates	Increased risk of mortality

ANCA; anti-neutrophil cytoplasmic autoantibodies, ESKD; End Stage Kidney Disease, EOS; End of Study, eGFR estimated glomerular filtration rate (mL/min/1.73 m<sup>2</sup>), HR; hazard ratio, RPGN; rapidly progressive glomerulonephritis, RRT; Renal replacement therapy, SD; Standard deviation, UK; United Kingdom, USA; United States of America

**Supplementary Table S3:** When applying sensitivity analyses with restricted follow-up to 1 and 2 years from the time of diagnosis, multivariate models show comparable hazard ratios when adjusting for ANCA status, gender, eGFR at diagnosis, age and induction therapy.

ESKD at 1 year follow up			ESKD at 2 years of follow up		
Variable	HR (95% CI)	P value	Variable	HR (95% CI)	P value
ANCA status	5.18 (2.00, 13.43)	<0.001	ANCA status	6.30 (2.36, 16.83)	<0.001
Gender	0.91 (0.40, 2.09)	0.83	Gender	0.96 (0.42, 2.19)	0.93
eGFR at diagnosis	0.98 (0.95, 1.00)	0.09	eGFR at diagnosis	0.99 (0.96, 1.01)	0.27
Age	0.98 (0.96, 1.00)	0.11	Age	0.98 (0.96, 1.01)	0.18
Induction Therapy	0.84 (0.26, 2.74)	0.77	Induction Therapy	1.00 (0.31, 3.26)	1.00

ANCA; anti-neutrophil cytoplasmic autoantibodies, CI; Confidence Intervals (95%), eGFR; estimated glomerular filtration rate (ml/min.1.73m<sup>2</sup>), ESKD; End Stage Kidney Disease, HR; Hazard ratio

**Supplementary Table S4:** Meta-analysis results reporting the unadjusted relative risk ratio and moderate to large degree of heterogeneity between studies. Not applicable (NA) results are due to insufficient data to create an estimate for the I<sup>2</sup> or tau<sup>2</sup> values.

Features	N	Proportion		RR [95% CI]	p-value	I <sup>2</sup> [95% CI]	τ <sup>2</sup>
		ANCA -ve	ANCA +ve				
Proportion of Males	9	53.30%	50.90%	1.19 [0.94 - 1.5]	0.156	0.53 [0.01 - 0.78]	6.24x10 <sup>-2</sup>
Mortality	8	20.80%	21.50%	1.22 [0.63 - 2.38]	0.554	0.57 [0.05 - 0.8]	4.99x10 <sup>-1</sup>
ESKD	7	43.10%	20.40%	2.28 [1.42 - 3.65]	0.001	0.62 [0.14 - 0.83]	2.37x10 <sup>-1</sup>
Relapse	2	16.30%	33.30%	0.49 [0.25 - 0.97]	0.039	0 [NA]	0
RRT at Presentation	7	46.30%	37.10%	1.23 [0.78 - 1.93]	0.374	0.72 [0.39 - 0.87]	2.21x10 <sup>-1</sup>
Berden – Crescentic	5	35.40%	28.30%	1.22 [0.79 - 1.88]	0.376	0 [0 - 0.79]	6.07x10 <sup>-2</sup>
Berden – Focal	5	26.30%	38.30%	0.85 [0.58 - 1.23]	0.380	0 [0 - 0.79]	0
Berden - Mixed	5	27.30%	24.80%	1.03 [0.69 - 1.53]	0.901	0.03 [0 - 0.8]	2.18x10 <sup>-2</sup>
Berden - Sclerosed	5	11.10%	8.60%	1.22 [0.63 - 2.35]	0.553	0 [0 - 0.79]	0
Renal Limited Disease	1	22%	5.90%	2.62 [1.3 - 5.27]	0.007	NA	NA
Features - Extra Renal	4	87.90%	96.30%	1 [0.96 - 1.04]	0.922	0.39 [0 - 0.79]	3.93x10 <sup>-6</sup>
Features Neurological	6	17.10%	14.30%	0.83 [0.31 - 2.19]	0.705	0.59 [0 - 0.83]	8.12x10 <sup>-1</sup>
Features - Cutaneous	7	32.30%	18.70%	1.33 [0.86 - 2.06]	0.201	0.71 [0.37 - 0.87]	1.98x10 <sup>-1</sup>
Features - ENT	7	22.20%	30.80%	0.37 [0.16 - 0.85]	0.020	0.65 [0.21 - 0.84]	6.38x10 <sup>-1</sup>
Features – Ophthalmic	6	1.40%	12.10%	0.23 [0.08 - 0.62]	0.004	0 [0 - 0.75]	0
Features - Respiratory	9	39.60%	42.30%	0.72 [0.55 - 0.94]	0.017	0.52 [0 - 0.77]	6.17x10 <sup>-2</sup>
Features - Systemic	5	36.20%	42.50%	0.7 [0.45 - 1.09]	0.115	0.56 [0 - 0.84]	1.05x10 <sup>-1</sup>

ANCA; anti-neutrophil cytoplasmic autoantibodies, ESKD; End Stage Kidney Disease, CI; Confidence Intervals (95%), ENT; Ears, nose and throat, I<sup>2</sup> (measure of heterogeneity), N; number, RR; relative risk, RRT; Renal replacement therapy, τ<sup>2</sup> (Measure of variance of true effect size)