Modification of the Renal Risk Score in ANCA Associated Glomerulonephritis improves prediction further

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Background

Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitides are multiorgan autoimmune disorders. Renal involvement is very common and disease presentation heterogeneous. Reliable prediction tools are needed to improve prognostication and personalisation of treatment. We aimed to validate and update the Renal Risk Score (RRS) [1] and explore other factors in renal survival in the largest cohort ever assembled.

Results

Of a total of 1591 patients, 1439 were included in the final analyses (959 in the development cohort, 52% male, median age 64 years, median follow-up 3.6 years, Supplementary Tables 1&2).

The RRS demonstrated a discrimination of C=0.800, comparable to the original cohort (Supplementary Table 3).

Reweighing, we found an additional useful cut-off for kidney function and further replaced glomerular filtration rate with serum creatinine which provided a higher reliability.

We modified the score creating four risk groups with an additional continuous model to supply risk percentages and groups. The new risk score replaces eGFR with creatinine and adds a second cut off (C0: <250 µmol/L, C1: 250-450 µmol/L, C2: >450 µmol/L). The model concordance was C=0.831 (C=0.815 in validation), as well as further splitting the *high* risk group into *high* and *very high* because of clear differences in survival.

	n (%)	β	HR	Points
Creatinine (µmol)				
C0: < 250	534 (55.7)	Ref		0
C1: 250 – 450	241 (25.1)	0.661	1.94 (1.30-2.89)	4
C2: > 450	184 (19.2)	1.886	6.59 (4.59-9.45)	11
Normal Glomeruli (%)				
N0: > 25	590 (61.5)	Ref		0
N1: 10 - 25	177 (18.5)	0.650	1.92 (1.30-2.82)	4
N2: < 10	192 (20.0)	1.199	3.32 (2.35-4.69)	7
IFTA (%)				
T0: < 25	469 (48.9)	Ref		0
T1: ≥ 25	490 (51.1)	0.527	1.69 (1.28-2.26)	3

Points	Group
0-4	Low
5-11	Moderate
12-18	High
21	Very High

Tables

Modified RRS, its coefficients, points and risk groupings.

Conclusion

We demonstrated the out-of-sample validity of the RRS and propose a modification of the score to improve prognostication and risk stratification for treatment and clinical trials. We believe that the risk score will be able to provide reliable predictions of renal survival and assist in decision making to balance benefits and risks of aggressive immunosuppression.

Materials and methods

We investigated a retrospective multicentre international longitudinal cohort from referral centres and registries around the world (Angers, Baltimore, London, Manchester, Mexico City, Prague, Preston, Salford, Uludağ, and the Irish and Scottish registries).

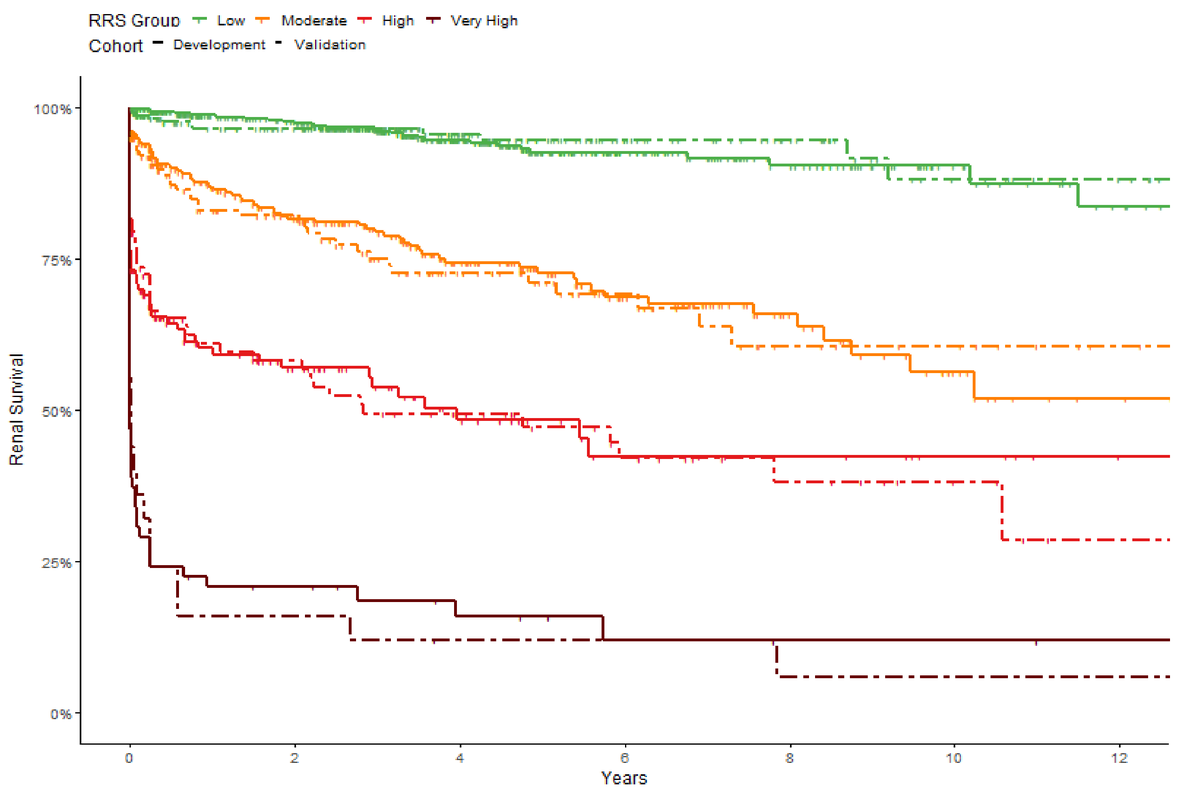
Included were patients with a biopsy proven ANCA associated glomerulonephritis (GN).

The primary endpoint was end stage kidney disease (ESKD) defined as renal replacement therapy (RRT) for at least 12 weeks and continued until last follow up. Patients were censored at last follow-up.

Kaplan-Meier estimates and Harrell's C were used to assess model performance. Cox Proportion Hazards were used to reweigh risk factors and develop a modified scoring system, with points assigned proportional to the parameters beta coefficient.

The Renal Risk Score was calculated for each patient using the estimated glomerular filtration rate (eGFR) at presentation (G0: eGFR>15 ml/min/1.73m^2, G1: eGFR≤15 ml/min/1.73m^2), the percentage of normal glomeruli in the kidney biopsy (N0: normal >25%, N1: normal 10%-25%, N2: <10%) and the simplified cut-off for tubular atrophy and interstitial fibrosis (T0: IFTA none, mild (or <25%), T1: IFTA mild to moderate – severe (or ≥25%)). Normal glomeruli were defined as glomeruli without any scarring, crescents or fibrinoid necrosis within in the tuft.

Each parameter was assigned points (G1=3, N1=4, N2=6, T1=2, G0=N0=T0=0) and summed, creating a total score and risk groups: low (0), moderate (2 - 7), and high (8 - 11 points).



Figure

Kaplan Meier plot of the modified RRS in the development and validation cohorts. There was strong agreement between cohorts for each risk group.

Future work

- App for bedside use (currently in proof of concept)
- Treatment pathway stratification by risk (trial pending sponsorship)

References

[1] Brix, Silke R., et al. "Development and validation of a renal risk score in ANCA-associated glomerulonephritis." *Kidney international* 94.6 (2018): 1177-1188.

eSupplement

github.com/sgbstats/ANCA

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Position in Translational Pathway

D1	D2	D3	D4	T1	T2	T3	T4

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