Evaluating renal outcome of ANCA-associated renal vasculitis: comparative study of two histopathological scoring systems

X.-N. An, Z.-N. Wei, X.-Y. Yao, J. Xu, W.-T. Qian, X.-X. Pan, P.-Y. Shen, H. Shi, W. Zhang, X.-N. Chen, N. Chen, Y.-X. Chen

Department of Nephrology, Ruijin Hospital affiliated to Shanghai Jiaotong University, School of Medicine, Shanghai, China.

*Xiao-Ning An, MD**
*Zhao-Nan Wei, MD**
*Xiang-Yun Yao, MD**
Jing Xu, MD
Wen-Ting Qian, MD
Xiao-Xia Pan
Ping-Yan Shen, MD
Hao Shi, MD
Wen Zhang, MD
Xiao-Nong Chen, MD
Nan Chen
Yong-Xi Chen, MD, PhD

**These authors contributed equally.*

Please address correspondence to:
Jing Xu,
Department of Nephrology, Ruijin Hospital affiliated to Shanghai Jiaotong University, School of Medicine, No. 197 Ruijin Er Rd., Shanghai 200025, China.
E-mail: xjjesse@126.com

or

Yong-Xi Chen,
(address as above)
E-mail: rickychen@sjtu.edu.cn

Received on April 5, 2020; accepted in revised form on June 15, 2020.

Clin Exp Rheumatol 2021; 39 (Suppl. 129): S39-S45.

Key words: antineutrophil cytoplasmic antibody, renal vasculitis, renal risk score, chronicity score, outcome

Funding: supported by grants from the National Natural Science Foundation (no. 81470041, no. 81000285).

Competing interests: none declared.

ABSTRACT

Objective. *Renal risk score (RRS) and chronicity score (CS) are both newly proposed tools to predict end stage renal disease (ESRD) which could be applicable in antineutrophil cytoplasmic antibody (ANCA)-associated renal vasculitis patients. Their predictive value has not been fully studied and compared.*

Method. *252 patients with newly biopsy-proven ANCA-associated renal vasculitis were retrospectively studied at the Department of Nephrology, Ruijin Hospital, China. Patients were evaluated with RRS and CS for clinical factors, pathological lesions and outcome. Their predictive value of renal survival was also compared.*

Result. *The median RRS score point at diagnosis was 6 (interquartile range [IQR] 0-9) and CS score point was 4 (IQR 3-7). In accordance with severity of RRS category and CS grade, percentage of hypertensive patients, dialysis dependency, and level of proteinuria increased accordingly. Significant differences were found regarding dialysis dependency within RRS and CS groups ($p<0.001$ and $p<0.01$ respectively). The addition of RRS or CS scoring scheme to the base model of dialysis dependency significantly improved discrimination. The C statistic, integrated discrimination improvement and net reclassification improvement were significantly increased by adding either RRS/CS or both. Furthermore, RRS had better ROC.*

Conclusion. *Among ANCA-associated renal vasculitis patients, RRS and CS achieved similar discrimination, but the discrimination of RRS was superior.*

Introduction

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of autoimmune disorders including granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) and their localised forms (1). Renal involvement of AAV, which is also known as ANCA-associated renal vasculitis, occurs in more than half of the AAV patients at disease onset (2). Despite of novel therapeutical approaches, the prognosis of patients with ANCA-associated renal vasculitis remains unsatisfactory (3). Given this background, identification of predictive factors for renal survival and outcome is important to improve prognosis.

The prognostic value of renal biopsy in ANCA-associated renal vasculitis is widely known as pathological lesions provide insight details for renal outcome in those patients. In 2010 Berden *et al.* (4) proposed a histopathologic classification for ANCA-associated renal vasculitis which consisted of four categories depending on the percentages of glomerular lesions. The classification has been proven clinically applicable but further modifications are warranted (5-7).

Recently several studies have been published using either newly proposed renal risk score (RRS) (8) or chronicity score (CS) (9, 10) to predict renal outcome in ANCA-associated renal vasculitis patients. RRS is a tool specifically designed to predict end stage renal disease (ESRD) in ANCA-associated renal vasculitis patients while CS is designed to report histopathological changes among primary and secondary glomerular diseases. Both of these scoring systems proved to be applicable in small cohorts, but the predictive value of these approaches remains incomparable due to variation in the studying population. We therefore performed a comparative study using RRS and CS to evaluate their predictive val-

Table I. Baseline characteristics of the patients.

Variables	Value
Male (n, %)	113 (44.8%)
Age (yr, mean ± SD)	57.5 ± 14.2
p-ANCA/MPO-ANCA positivity (n, %)	222 (88.1%)
BVAS (median, IQR)	19 (16-23)
Serum creatinine (μmol/L, median, [IQR])	245 (128-484)
eGFR (ml/min, median, [IQR])	20.3 (9.2-45.3)
Proteinuria (mg/d, median, [IQR])	1260 (619.5-2315.5)
Follow-up (mo, mean ± SD)	63.9 ± 49.5

eGFR: estimated glomerular filtration rate; BVAS: Birmingham Vasculitis Assessment Score; IQR: interquartile range.

ue in ANCA-associated renal vasculitis patients so as to provide further data to predict renal outcome in those patients at baseline.

Methods

Patient selection

252 patients with newly diagnosed ANCA-associated renal vasculitis who underwent renal biopsy at the Department of Nephrology, Ruijin Hospital affiliated to Shanghai Jiaotong University, School of Medicine between 1997 and 2018 were enrolled in the current study. Inclusion criteria were described as our previous report (5), briefly: (1) ANCA was detected in the sera, (2) fulfilling the criteria of the Chapel Hill Consensus Conference definition for AAV(1), (3) underwent renal biopsy with ≥10 glomeruli found in the renal biopsy specimen, and (4) follow-up for at least 12 months (including patients who died within the first 12 months due to active vasculitis or vasculitis complications). Patients with secondary vasculitis or comorbid renal diseases were excluded. Being a retrospective study, all subjects were treated with standard care, and all data were retrospectively obtained from our electronic database. This study was approved by the hospital review board to screen out patients.

ANCA analysis and clinical data

All patients had been tested for the presence of ANCA by indirect immunofluo-

Table II. Evaluation of ANCA-associated renal vasculitis patients with RRS and CS.

	RRS Group (n, %)			
	Low (n=68)	Median (n=86)	High (n=98)	*p*
Hypertension (*n*, %)	28 (41.2)	53 (61.6)	77 (78.6)	<0.001
SBP (mmHg, median, [IQR])	128 (120-135)	136 (120-158)	140 (130-160)	<0.001
DBP (mmHg, median, [IQR])	80 (70-81)	80 (70-85)	80 (73-90)	<0.01
Renal presentation				
Serum creatinine (μmol/L, median, [IQR])	111 74-162)	241 (144-407)	444 (313.5-648)	<0.001
eGFR (ml/min, median, [IQR])	57.2 (31.9-92.1)	20.4 (9.5-38.5)	10.6 (6.0-15.3)	<0.001
Proteinuria (mg/d, median, [IQR])	668 (251-1260)	1177 (672.5-1840)	1944 (1102-3240)	<0.001
Dialysis at diagnosis (*n*, %)	0 (0)	13 (15.1)	37 (37.8)	<0.001
Renal histology (median, [IQR])				
Total glomeruli	22 (17.3-31)	21 (14-31.5)	21 (15-30)	NS
Normal glomeruli	14 (9-21)	5 (1.5-8)	0 (0-1)	<0.001
Sclerotic glomeruli	2 (0-3)	3 (1-6.5)	6 (2-1.25)	<0.001
BVAS (median, IQR)	18 (14-21)	20 (16-26)	20 (17-24)	<0.01
	CS Grade (n, %)			
	Minimal (n=13)	Mild (n=120)	Moderate (n=67)	Severe (n=52)	*p*
Hypertension (*n*, %)	4 (30.8)	68 (56.7)	47 (70.1)	39 (75)	<0.01
SBP (mmHg, median, [IQR])	120 (102.5-135)	130 (120-151)	140 (126-151)	140 (121.3-158.8)	<0.05
DBP (mmHg, median, [IQR])	75 (70-90)	80 (70-85)	80 (73-90)	80 (71.3-90)	NS
Renal presentation					
Serum creatinine (μmol/L, median, [IQR])	184 (79.5-257)	189 (94-408)	271 (142-546)	382 (242.5-622.8)	<0.001
eGFR (ml/min, median, [IQR])	23.4 (18.4-101)	28.7 (11.2-64.1)	16.4 (8.2-39.6)	11.2 (6.5-20.5)	<0.001
Proteinuria (mg/d, median, [IQR])	1420 (272.5-2999)	967 (469-1604)	1383 (806-2956)	1905 (924.8-3105.8)	<0.001
Dialysis at diagnosis (*n*, %)	1 (7.7)	21 (17.5)	11 (16.4)	17 (32.7)	NS
Renal histology (median, [IQR])					
Total glomeruli	17 (10.5-21)	22 (16-30)	23 (14-34)	24 (18-30)	NS
Normal glomeruli	11 (1.5-18.5)	6 (0-14)	4 (0-8)	0 (0-4)	<0.001
Sclerotic glomeruli	0 (0-0.5)	1 (0-3)	5 (2-9)	13.5 (7.3-17)	<0.001
BVAS (median, IQR)	21 (18-24)	20 (16-23.8)	18 (16-23)	18 (16-21)	NS

RRS: renal risk score; CS: chronicity score; SBP: systolic blood pressure; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; BVAS: Birmingham Vasculitis Assessment Score.
Values are number (percent) or median (interquartile range). *p* value applies to the variables within RRS/CS groups.

rescence and ELISA (Euroimmun AG), as previously reported (11-15).

The Chronic Kidney Disease Epidemiology Collaboration Creatinine Equation (CKD-EPI) was used to calculate estimated GFR(eGFR) (16). Birmingham Vasculitis Assessment Score (BVAS) 2003 was used to evaluate disease activity at initial presentation (17). Renal outcome was defined as end stage renal disease (ESRD) caused by AAV requiring renal placement therapy including haemodialysis, renal transplantation or peritoneal dialysis.

Renal histology

Renal specimens were processed for both light microscopy and electron microscope as we previously reported (5, 12, 14). All the specimens met the requirement of a minimum of 10 whole glomeruli per biopsy.

Biopsies were independently scored by two pathologists (XXP and JX) blinded to the clinical data and according to the previously standardised definitions. Differences in scoring between the two pathologists were resolved by re-reviewing the biopsies by a third pathologist (QC) and coming to a consensus.

For the assessment of Chronicity Score (CS), calculating was made including glomerulosclerosis (GS score), interstitial fibrosis (IF score), tubular atrophy (TA score) and arteriosclerosis (CV score) as reported (10).

For the assessment of Renal Risk Score (RRS), calculating was made including percentage of normal glomeruli (N), tubular atrophy/interstitial fibrosis (T) and renal function at time of diagnosis (GFR) as proposed (17).

Definitions for normal glomeruli, crescents, global sclerosis and histological classification were made according to the definition proposed by Berden *et al*. (4). We combined patients in "Mixed" and "Crescentic" Classes while conducting further analysis.

Statistics

Statistical analysis was performed using SPSS 13.0 (SPSS Inc.) and Stata 12 (StataCorp LP). Data with normal distribution were summarised as mean ± SD. Data without normal distribution were summarised as median and interquartile range. Comparisons were made using the Student *t* test or 1-way ANOVA for continuous variables and by the χ^2 test for categorical variables as required. The cumulative renal survival rates were measured by the Kaplan-Meier method, and differences between survival curves were compared with the log-rank test. The discrimination ability in predicting dialysis dependency was assessed using the area under the receiver operating characteristic curve (AUC). We calculated the difference (C statistics), net reclassification improvement (NRI) and integrated discrimination improvement (IDI) (18). IDI and NRI were performed using NRI and IDI programs for Stata as reported (19). A *p*-value <0.05 was considered statistically significant.

Table III. Distribution of RRS risk groups.

RRS Risk factors (score point)	No. of patients (n=252) *n* %	Sum of score point
Percentage of normal glomeruli (N)		6 (0-9)
N0 (0)	102 (40.5)	
N1 (4)	44 (17.5)	
N2 (6)	106 (42.1)	
Tubular atrophy/interstitial fibrosis (T)		
T0 (0)	139 (55.2)	
T1 (2)	113 (44.8)	
Renal function at time of diagnosis (GFR)		
G0 (0)	151 (59.9)	
G1 (3)	101 (40.1)	

RRS: renal risk score.
Patient numbers in each RRS risk group (normal glomeruli, tubular atrophy/interstitial fibrosis, and eGFR) are expressed as value and percentage. Score point of total RRS score point are expressed as median (IQR).

Table IV. Distribution of CS tissue compartment.

	No. of patient (n=252)				
	Score 0 (*n*, %)	Score 1 (*n*, %)	Score 2 (*n*, %)	Score 3 (*n*, %)	Total CS
Glomerulosclerosis (GS)	93 (36.9)	51 (20.2)	49 (19.4)	59 (23.4)	4 (3-7)
Interstitial fibrosis (IF)	10 (4.0)	129 (51.2)	58 (23.0)	55 (21.8)	
Tubular atrophy (TA)	13 (5.2)	128 (50.8)	57 (22.6)	54 (21.4)	
Arteriosclerosis (CV)	136 (54.0)	116 (46.0)	/	/	

CS: chronicity score.
Patient numbers in each CS category (glomerulosclerosis, interstitial fibrosis, tubular atrophy and arteriosclerosis) are expressed as value and percentage. Score point of total CS score point is expressed as median (IQR).

Table V. Renal outcome stratified by RRS and CS.

	RRS			CS		
Group	Dialysis dependency (*n*, %)	*p*	Group	Dialysis dependency (*n*, %)	*p*
Low (n=68)	2 (2.9)	<0.001	Minimal (n=13)	1 (7.7)	<0.01
Medium (n=86)	22 (25.6)		Mild (n=120)	25 (20.8)	
High (n=98)	47 (48.0)		Moderate (n=67)	21 (31.3)	
			Severe (n=52)	24 (46.2)	

RRS: renal risk score; CS: chronicity score.
Patients required dialysis (including those who had underwent renal transplantation) in each RRS/CS group. Numbers are expressed as value and percentage. *p* value applies to the variable within RRS/CS groups.

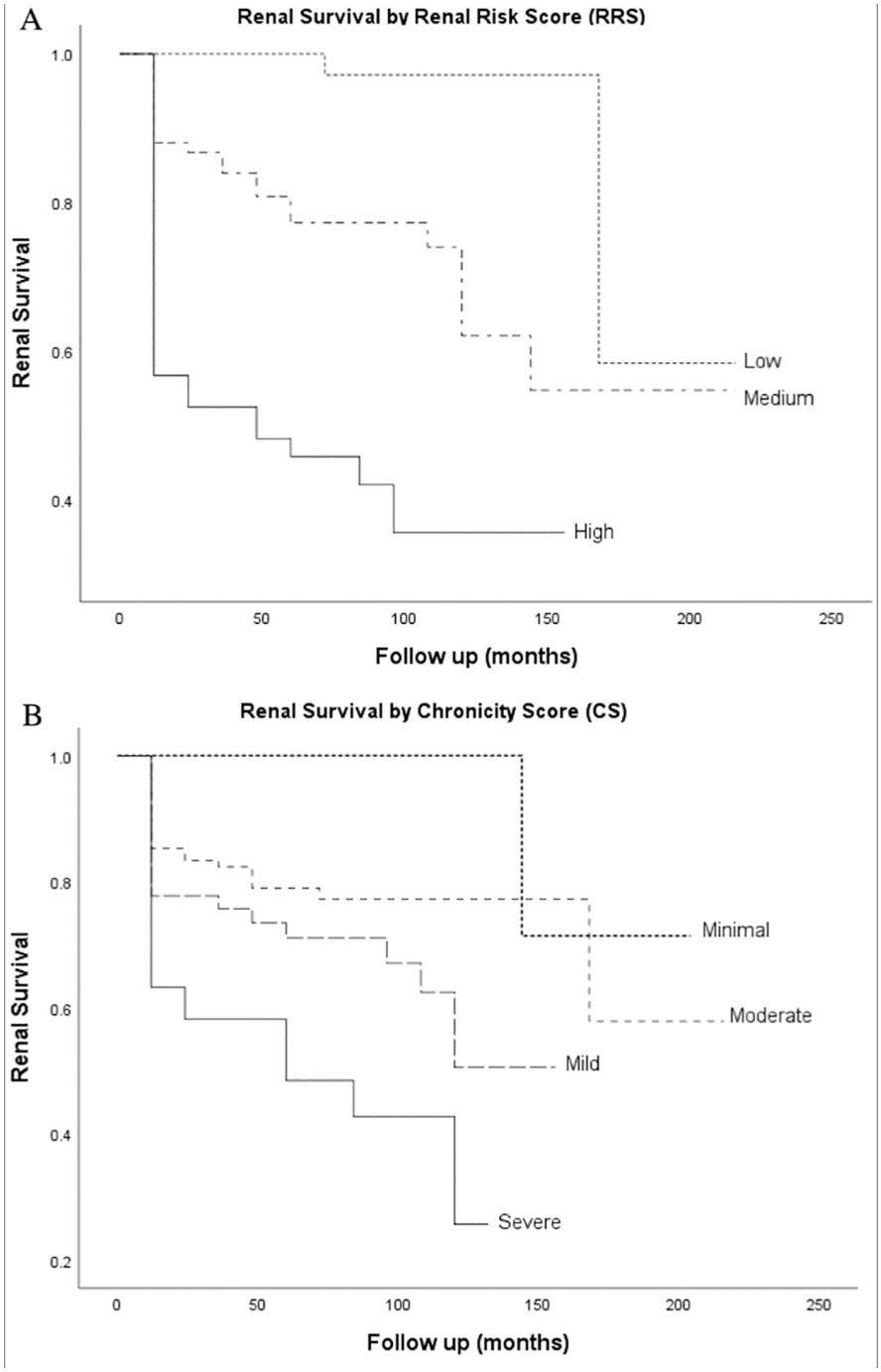

Fig. 1. Renal outcome by RRS and CS.
(**A**) Kaplan-Meier analysis of renal outcome using RRS scoring system. Renal survival rate is best in "Low" grade while worst in "High" grade. (**B**) Kaplan-Meier analysis of renal outcome using CS scoring system. Renal survival rates deteriorate in a descending order of "Minimal", "Moderate", "Mild" and "Severe".

Results

Demographic, clinical and laboratory presentations of the patients

There were 252 ANCA-associated renal vasculitis patients enrolled in current study, including 212 MPA, 12 GPA, 4 EGPA and 24 renal limited vasculitis (RLV). BVAS at the time of biopsy was 19 (interquartile range [IQR] 16-23). Baseline characteristics were summarised in Table I.

Evaluating renal involvement with RRS and CS

Fifty (19.8%) patients required dialysis at disease onset. The median RRS score at diagnosis was 6 (IQR 0-9) and CS score was 4 (IQR 3-7).

By categorising patients with RRS and CS, our results showed that in accordance with increase of RRS/CS sum scores, percentage of hypertensive patients, level of proteinuria and percentage of dialysis dependency increased accordingly (Table II). The distribution of RRS risk groups and CS tissue compartment were summarised in Table III and Table IV.

Evaluating renal outcome with RRS and CS

During up to 217 months of follow-up (mean 63.9 months), 71 (28.2%) patients progressed to end stage renal disease (ESRD) and required renal replacement therapy. ESRD stratified by RRS and CS were summarised in Table V. Significant differences were found regarding dialysis dependency within RRS and CS groups ($p<0.001$ and $p<0.01$ respectively). Forty-four patients (17.5%) achieved complete renal remission and rest 137 (54.4%) remained renal insufficiency. Kaplan-Meier analysis showed that renal outcome deteriorated in accordance with increase of RRS sum scores (Fig. 1A, $p<0.001$). By classifying with CS, renal outcome was best in "Minimal" grade and worst in "Severe" grade. Significant differences were found within different groups with CS (Fig. 1B, $p<0.01$). In our study, patients with "Moderate" grade had better renal outcome than those with "Mild" grade without statistical significance.

Cross-tabulation analysis of RRS and CS

By cross-tabulating, categories classified with CS and RRS shown in Table VI revealed that 28 patients (28/252, 9.9%) with CS "Minimal" or "Mild" grade were classified as RRS "High" while no patients with RRS "Low" were classified as CS "Severe" grade. The rest of patients were classified in similar categories with RRS or CS scores.

Predictive values of RRS and CS

The C statistic of the predictive models was 0.828 (95% CI, 0.775-0.880) for developing ESRD required renal

Table VI. Cross-tabulation analysis of patients classified by RRS *vs*. CS.

Scoring System	CS Count (*n*, %)				Total (CS)
	Minimal	Mild	Moderate	Severe	Count (*n*, %)
RRS					
Low	8 (3.2)	56 (22.2)	4 (1.6)	0 (0)	68 (27.0)
Medium	4 (1.6)	37 (14.7)	31 (12.3)	14 (5.6)	86 (34.1)
High	1 (0.4)	27 (10.7)	32 (12.7)	38 (15.1)	98 (38.9)
Total (RRS) Count (*n*, %)	13 (5.2)	120 (47.6)	67 (26.6)	52 (20.6)	252 (100)

RRS: renal risk score; CS: chronicity score.
Patients were both classified by RRS and CS. Number of patients are expressed as value and percentage.

Table VII. Improvement in predicting renal outcome by adding RRS, CS to a model containing clinical risk factors.

Model	C statistic (95% CI)	*p*	IDI	NRI
Base model (reference)	0.828 (0.775-0.880)			
Base model plus RRS	0.883 (0.840-0.927)	0.002	<0.001	0.004
Base model plus CS	0.854 (0.805-0.903)	0.03	0.001	0.300
Base model plus RRS and CS	0.896 (0.855-0.937)	<0.001	<0.001	0.004

NRI: net reclassification improvement; IDI: integrated discrimination improvement; RRS: renal risk score; CS: chronicity score.
Base model included age, gender, eGFR, BVAS, proteinuria, hypertension, systolic blood pressure, diastolic blood pressure, anemia, ESR, albumin, C3 and C4.
The C statistic measures concordance between model-based risk estimates and observed dialysis dependency (including renal transplantation).
NRI and IDI measure the incremental prognostic effect that either RRS/CS or both will have when added to base model.
p value applies to difference in C statistics between base model and base model plus RRS, CS or both.

Table VIII. AUC for different scoring systems/classification to predict renal outcome.

Criteria	AUC	95% CI	*p*
RRS	0.742	0.679-0.804	<0.001
CS	0.641	0.564-0.717	0.001
Histopathological Classification	0.587	0.515-0.659	0.031

AUC: area under the receiver operating characteristic curve; RRS: renal risk score; CS: chronicity score.
AUCs showed the predictive ability for dialysis dependency for RRS, CS or histological classification.

replacement therapy. The addition of RRS or CS scoring scheme to the model significantly improved discrimination (Table VII). The IDI and NRI were significantly increased by adding either or both of RRS and CS scoring schemes.

Comparison of RRS and CS with histological classification

In the sensitivity analysis, we assessed the robustness of our study results by using ROC curves (Fig. 2) to compare RRS, CS together with histological classification, which is a classical classification of ANCA-associated renal vasculitis. Our results showed that when each set of criteria was applied to dialysis dependency (including renal transplantation), RRS and CS both showed adequate and similar discrimination, but significantly greater discrimination than histopathological classification (Table VIII).

Discussion

Renal involvement is the most common manifestation in patients with AAV. According to our previous report and studies published elsewhere, renal survival is closely associated with patient prognosis and outcome (9, 15, 20-23). Renal histology not only reflects the activity and chronicity of the disease but provides insightful information regarding prognosis and treatment response as well. In light of important role of renal histology, categorising ANCA-associated renal vasculitis patients according to severity of renal histology and predicting their renal outcome would help to make therapeutical strategies.

Currently two scoring systems (RRS and CS) and one classification (2010 histopathological classification) have been proposed to predict renal outcome at baseline in ANCA-associated renal vasculitis patients. The 2010 histological classification has been validated in many series and proved to be clinical applicable, while the other two was recently introduced and validated in small populations. CS was introduced to provide a uniform reporting of histopathologic changes among different glomerulonephritis including ANCA-associated renal vasculitis. Similar to the 2010 histological classification, CS doesn't compromise clinical parameters like BVAS or serum creatinine. It focuses on chronic changes including glomerulosclerosis, tubular atrophy and interstitial fibrosis as chronic renal lesions regardless of aetiology of the diseases are strong predictors of renal outcome (10). In a recent study on epidemiology and clinical outcome of ANCA-associated renal vasculitis, Berti *et al*. (10) studied association between CS and renal outcome which showed that CS at diagnosis provided better stratification of renal prognosis than clinical diagnosis or ANCA serology. Though several studies point out ANCA serology is also an important factor to predict renal outcome in ANCA-associated renal vasculitis patients because PR3-ANCA vasculitis patients usually have better renal outcome than those with MPO-ANCA vasculitis (24-28). The study by Berti *et al*. highlighted important role of renal chronic lesions because lesions like crescents, fibrinoid necrosis and other active vasculitis injuries might progress to same chronic lesions regardless of subsets of AAV. Infiltrated T cells, monocytes or macrophages might also contribute to chronic lesions that affect renal outcome (29-32). In current study, our results show that patients with advanced CS scores are less likely to recover from renal injury and have worse re-

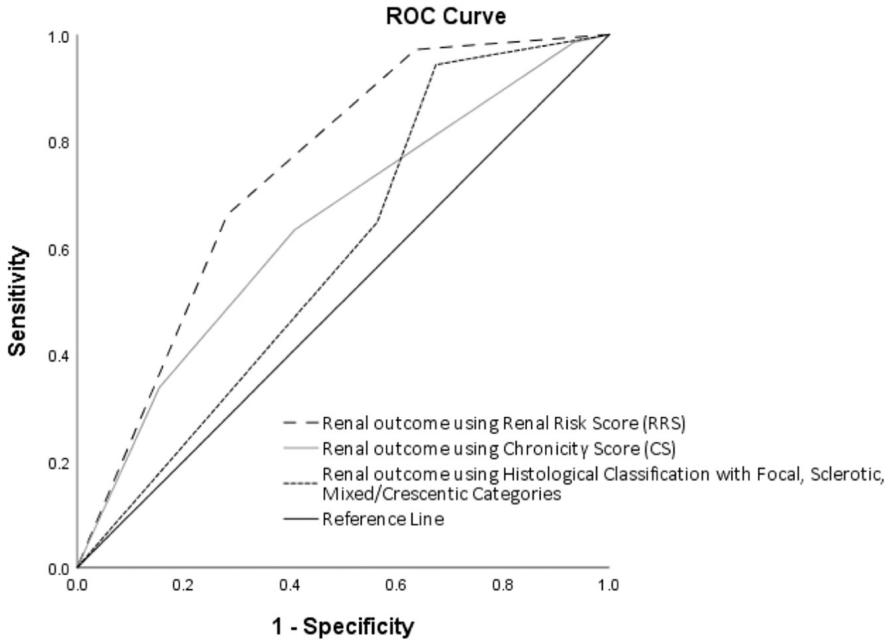

Fig. 2. ROC curves of different scoring systems/classification.
ROC curves of RRS, CS and histological classification using patients' renal outcome as reference.
For the evaluation with histological classification, we combine "Mixed" and "Crescentic" group together and classify the patients into "Focal", "Sclerotic" and "Mixed/Crescentic" Class.

nal outcome. The predictive value of CS supports the findings that chronic lesions are associated with adverse renal outcome in ANCA-associated renal vasculitis patients (33, 34).

RRS is another scoring system for ANCA-associated renal vasculitis patients. Different to histological classification or CS, RRS utilises renal histology and eGFR at baseline to predict renal outcome. In a study with 115 training cohorts and 90 validation cohorts, Brix and colleagues(8) found that patients with maximum score (N2T1G1) would eventually develop ESRD. In our study, 27/34 (79%) patients with maximum RRS score developed ESRD and 6/34 (18%) patients with same scoring category died of ESRD complication before starting dialysis. Our results suggest advanced RRS score correlate with worse renal outcome. In another study in ANCA-associated renal vasculitis patient with severe kidney failure, Lee *et al*. (35) demonstrated that low baseline renal function and severe renal scarring were associated with lower treatment response rate which highlighted the influence of both kidney function at baseline and renal histology on patients' treatment response and outcome. Similar data were also found by Smith and colleagues (36) in their Scottish cohort. All these data thus support kidney function at baseline is an important risk factor to predict renal prognosis in ANCA-associated renal vasculitis patients.

Compared with the 2010 histological classification, both CS and RRS add tubulointerstitial injury to the scoring system which demonstrate the important role of tubulointerstitial injury in predicting renal outcome. In the study focusing on rituximab therapy in ANCA-associated renal vasculitis patients, Berden *et al*. found renal tubular lesions were associated with renal outcome. Tubular atrophy was an independent predictor for renal outcome at 1 year (37). Other studies showed infiltrating T cells in the interstitium were significantly associated with serum creatinine at the time of renal biopsy. Our previous study and study published elsewhere demonstrate that ANCA-associated renal vasculitis patients with more severe tubulointerstitial injury would have worse renal outcome which further supports the important role of tubulointerstitial injury in predicting renal outcome (5, 38).

Current study is the first to compare predictive value of current scoring system/classification in ANCA-associated renal vasculitis patients. ROC analysis yielded AUC values of 0.74, 0.64, 0.59 for RRS, CS and histological classification respectively, indicating RRS has the best performance. Since both eGFR and tubulointerstitial injury are included in RRS, our results demonstrate the important role of these two parameters in predicting renal outcome in ANCA-associated renal vasculitis patients. Compared with histological classification, neither CS or RRS takes crescents as a parameter to predict renal outcome. Although cellular crescents usually represent active vasculitic lesions which require timely treatment, our previous meta-analysis showed that renal outcome in ANCA-associated renal vasculitis patients with crescentic lesions did not differ from those with mixed lesions (5). Role of crescentic lesions in ANCA-associated renal vasculitis patients therefore might not be as important as normal glomeruli or sclerotic glomeruli with regards to predict renal prognosis.

In conclusion, we validate clinical application of established scoring systems in predicting renal outcome in ANCA-associated renal vasculitis patients. By comparing predictive value of established scoring systems/classification, our results point out the important role of renal tubulointerstitial injury and eGFR at baseline in predicting renal prognosis.

References

1. JENNETTE JC, FALK RJ, BACON PA *et al*.: 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides. *Arthritis Rheum* 2013; 65: 1-11.
2. BOSCH X, GUILABERT A, ESPINOSA G, MIRAPEIX E: Treatment of antineutrophil cytoplasmic antibody associated vasculitis: a systematic review. *JAMA* 2007; 298: 655-69.
3. MONTI S, BOND M, FELICETTI M *et al*.: One year in review 2019: Vasculitis. *Clin Exp Rheumatol* 2019; 37 (Suppl. 117): S3-19.
4. BERDEN AE, FERRARIO F, HAGEN EC *et al*.: Histopathologic classification of ANCA-associated glomerulonephritis. *J Am Soc Nephrol* 2010; 21: 1628-36.
5. CHEN YX, XU J, PAN XX *et al*.: Histopathological classification and renal outcome in patients with antineutrophil cytoplasmic antibodies-associated renal vasculitis: A study of 186 patients and metaanalysis. *J Rheumatol* 2017; 44: 304-13.
6. TANNA A, PUSEY CD: The histopathological classification of ANCA-associated glomeru-

lonephritis comes of age. *J Rheumatol* 2017; 44: 265-7.
7. KRONBICHLER A, JAYNE DRW: Anca renal risk score: Is prediction of end-stage renal disease at baseline possible? *Kidney Int* 2018; 94: 1045-7.
8. BRIX SR, NORIEGA M, TENNSTEDT P *et al*.: Development and validation of a renal risk score in ANCA-associated glomerulonephritis. *Kidney Int* 2018; 94: 1177-88.
9. BERTI A, CORNEC-LE GALL E, CORNEC D *et al*.: Incidence, prevalence, mortality and chronic renal damage of anti-neutrophil cytoplasmic antibody-associated glomerulonephritis in a 20-year population-based cohort. *Nephrol Dial Transplant* 2019; 34: 1508-17.
10. SETHI S, D'AGATI VD, NAST CC *et al*.: A proposal for standardized grading of chronic changes in native kidney biopsy specimens. *Kidney Int* 2017; 91: 787-9.
11. CHEN YX, ZHANG W, CHEN XN *et al*.: Clinical analysis of ANCA-associated renal vasculitis patients with chronic dialysis. *Clin Exp Rheumatol* 2014; 32 (Suppl. 82): S5-10.
12. CHEN YX, ZHANG W, CHEN XN *et al*.: Propylthiouracil-induced antineutrophil cytoplasmic antibody (ANCA)-associated renal vasculitis versus primary anca-associated renal vasculitis: A comparative study. *J Rheumatol* 2012; 39: 558-63.
13. CHEN YX, ZHANG W, CHEN XN *et al*.: Application of rifle criteria in Chinese patients with ANCA-associated renal vasculitis. *Clin Exp Rheumatol* 2011; 29: 951-7.
14. CHEN YX, YU HJ, NI LY *et al*.: Propylthiouracil-associated antineutrophil cytoplasmic autoantibody-positive vasculitis: Retrospective study of 19 cases. *J Rheumatol* 2007; 34: 2451-6.
15. CHEN YX, YU HJ, ZHANG W *et al*.: Analyzing fatal cases of Chinese patients with primary antineutrophil cytoplasmic antibodies-associated renal vasculitis: A 10-year retrospective study. *Kidney Blood Press Res* 2008; 31: 343-9.
16. LEVEY AS, STEVENS LA, SCHMID CH *et al*.: A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150: 604-12.
17. FLOSSMANN O, BACON P, DE GROOT K *et al*.: Development of comprehensive disease assessment in systemic vasculitis. *Ann Rheum Dis* 2007; 66: 283-92.
18. PENCINA MJ, D'AGOSTINO RB, PENCINA KM, JANSSENS AC, GREENLAND P: Interpreting incremental value of markers added to risk prediction models. *Am J Epidemiol* 2012; 176: 473-81.
19. PENCINA MJ, D'AGOSTINO RB, SR, D'AGOSTINO RB, JR, VASAN RS: Evaluating the added predictive ability of a new marker: From area under the roc curve to reclassification and beyond. *Stat Med* 2008; 27: 157-72; discussion 207-12.
20. FLOSSMANN O, BERDEN A, DE GROOT K *et al*.: Long-term patient survival in ANCA-associated vasculitis. *Ann Rheum Dis* 2011; 70: 488-94.
21. WESTER TREJO MAC, FLOSSMANN O, WESTMAN KW *et al*.: Renal relapse in antineutrophil cytoplasmic autoantibody-associated vasculitis: Unpredictable, but predictive of renal outcome. *Rheumatology* (Oxford) 2019; 58: 103-9.
22. MUN CH, YOO J, JUNG SM, SONG JJ, PARK YB, LEE SW: The initial predictors of death in 153 patients with ANCA-associated vasculitis in a single Korean centre. *Clin Exp Rheumatol* 2018; 36 (Suppl. 111): S65-72.
23. PARK ES, AHN SS, JUNG SM, SONG JJ, PARK YB, LEE SW: Renal outcome of kidney-transplantation in Korean recipients with ANCA-associated vasculitis. *Clin Exp Rheumatol* 2018; 36 (Suppl. 111): S115-20.
24. JENNETTE JC, NACHMAN PH: ANCA glomerulonephritis and vasculitis. *Clin J Am Soc Nephrol* 2017; 12: 1680-91.
25. VAN DER GEEST KSM, BROUWER E, SANDERS JS *et al*.: Towards precision medicine in ANCA-associated vasculitis. *Rheumatology* (Oxford) 2018; 57: 1332-9.
26. HAUER HA, BAJEMA IM, VAN HOUWELINGEN HC *et al*.: Renal histology in ANCA-associated vasculitis: Differences between diagnostic and serologic subgroups. *Kidney Int* 2002; 61: 80-9.
27. CORNEC D, CORNEC-LE GALL E, FERVENZA FC, SPECKS U: ANCA-associated vasculitis - clinical utility of using ANCA specificity to classify patients. *Nat Rev Rheumatol* 2016; 12: 570-9.
28. CHANG DY, LI ZY, CHEN M, ZHAO MH: Myeloperoxidase-ANCA-positive granulomatosis with polyangiitis is a distinct subset of anca-associated vasculitis: A retrospective analysis of 455 patients from a single center in China. *Semin Arthritis Rheum* 2019; 48: 701-6.
29. KALLENBERG CG: Antineutrophil cytoplasmic autoantibody-associated small-vessel vasculitis. *Curr Opin Rheumatol* 2007; 19: 17-24.
30. JENNETTE JC, FALK RJ: ANCAs are also antimonocyte cytoplasmic autoantibodies. *Clin J Am Soc Nephrol* 2015; 10: 4-6.
31. CHEN YX, CHEN XN: Antineutrophil cytoplasmic antibodies-associated glomerulonephritis: from bench to bedside. *Chronic Dis Transl Med* 2018; 4: 187-91.
32. KAPLAN MJ: Role of neutrophils in systemic autoimmune diseases. *Arthritis Res Ther* 2013; 15: 219.
33. DE LIND VAN WIJNGAARDEN RA, HAUER HA, WOLTERBEEK R *et al*.: Clinical and histologic determinants of renal outcome in anca-associated vasculitis: A prospective analysis of 100 patients with severe renal involvement. *J Am Soc Nephrol* 2006; 17: 2264-74.
34. HAUER HA, BAJEMA IM, VAN HOUWELINGEN HC *et al*.: Determinants of outcome in anca-associated glomerulonephritis: A prospective clinico-histopathological analysis of 96 patients. *Kidney Int* 2002; 62: 1732-42.
35. LEE T, GASIM A, DEREBAIL VK *et al*.: Predictors of treatment outcomes in anca-associated vasculitis with severe kidney failure. *Clin J Am Soc Nephrol* 2014; 9: 905-13.
36. SMITH JR, METHVEN S, STEVENS KI, MACKINNON B, KIDDER D: Renal risk score performance in a cohort of scottish patients with ANCA-associated glomerulonephritis. *Kidney Int* 2019; 96: 1037.
37. BERDEN AE, JONES RB, ERASMUS DD *et al*.: Tubular lesions predict renal outcome in antineutrophil cytoplasmic antibody-associated glomerulonephritis after rituximab therapy. *J Am Soc Nephrol* 2012; 23: 313-21.
38. CHANG DY, WU LH, LIU G, CHEN M, KALLENBERG CG, ZHAO MH: Re-evaluation of the histopathologic classification of ANCA-associated glomerulonephritis: A study of 121 patients in a single center. *Nephrol Dial Transplant* 2012; 27: 2343-9.