Remission of proteinuria but not remission of hematuria is important for long-term renal prognosis in IgA nephropathy

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Introduction

It has been reported that the grade of proteinuria is important for the renal prognosis in IgA nephropathy, and the renal prognosis is favorable when urinary protein is controlled at below 0.3 g/day.1),2) On the other hand, hematuria is always noted in IgA nephropathy, but its association with the renal prognosis is controversial.3),4) In Japan, remission criteria were proposed and proteinuria below 0.3 g/day (g/g.cr) with a red blood cell count in urinary sediment below 5/HPF detected 3 times or more for 6 months or longer was defined as complete remission(CR). When only proteinuria meets the remission criteria, the condition was defined as partial remission (PR). 5)

Objectives

Based on the remission criteria proposed in Japan, we compared factors involved in the remission of proteinuria and remission of both proteinuria and hematuria, and investigated differences in the renal prognosis between these 2 types.

Methods

- Design: retrospective cohort study
- Patients: 632 patients diagnosed with IgA nephropathy between 1980 and September 2012 and followed for one year or longer at our hospital.
- Parameters investigated: age, gender, MAP, eGFR(ml/min/1.73m^2), excretion of urinary protein, hematuria score, histological findings using oxford classification (M.E.S.T.) at the time of kidney biopsy, and treatment methods.
-Outcome:
  1.remission of only proteinuria (PR)and both of proteinuria and hematuria (CR).
  2.50% decrease of eGFR as compared with baseline data among the two groups (group A ; PR, group B; CR)
- Statistics: cox's hazard proportional model was used for analysis of both types of remission. Kaplan-Meire method and logrank test was used for analysis of renal prognosis. P<0.05 was considered as significant.

Results

Patient's characteristics   n=632

	%	Mean±S.D.	Median (range)
Gender (male %)	46		
Age (ys)		36.8 ± 14.7	35.2 (13.5 – 75.4)
MAP (mmHg)		90.5 ± 13.6	89.3 (57.3 – 149.0)
sCr (mg/dL)		0.92 ± 0.42	0.80(0.4 – 6.2)
eGFR (ml/min/1.73m^2)		76.2 ± 25.9	75.6 (9.1 - 166.1)
UP(g/d)		0.93 ± 1.26	0.6 (0.0 - 12.0)
Hematuria score*		2.4 ± 1.7	2 (0 - 5)
Duration from occurrence of disease until I diagnosis (years)		4.9±7.3	2.3 (0.1 – 50.1)
Oxford classification M(0)	86		
E (0)	82		
S (0)	43		
T (0)	85		
Cres (0)	81		
Treatment PSL (%)	28		
RAS I (%)	49		
Anti-platelet agents(%)	66		
tonsillectomy (%)	3		
no therapy(%)	21		
Observational periods (years)		10.6±8.3	7.9 (1.0-35.8)

*Hematuria score: U-RBC/HPF <5/HPF=0, 5-9/HPF=1, 10-29/HPF=2, 30-49/HPF=3, >50/HPF=4, macrohematuria=5,

### Remission of proteinuria (PR) or both hematuria and proteinuria (CR)
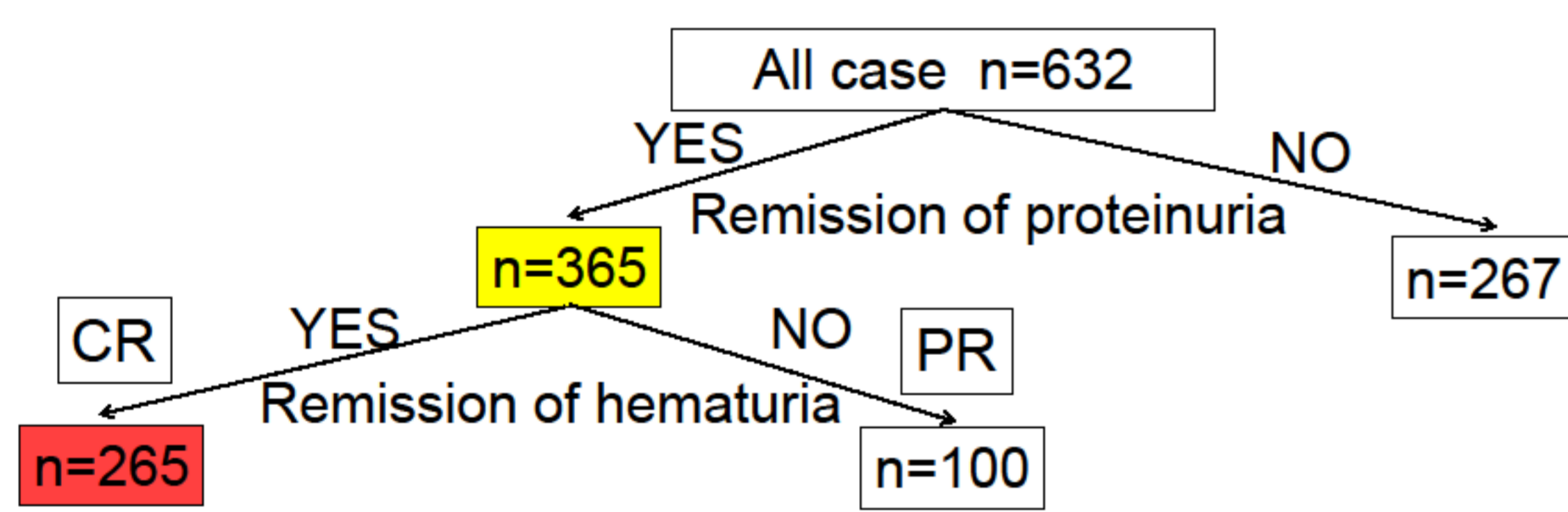
Factors associated with remission of proteinuria (PR)

	univariate analysis			multivariate analysis		
	HR	95%CI	p value	HR	95%CI	p value
gender(male1)	0.73	0.59-0.89	0.0025	0.90	0.71-1.12	0.3420
age(every 10y)	0.95	0.88-1.03	0.2015	1.23	1.15-1.41	<.0001
MAP(every10mmHg)	0.83	0.76-0.90	<0.0001	0.94	0.85-1.06	0.2237
eGFR(every10ml/min/1.73m^2)	1.10	1.06-1.15	<0.0001	1.05	0.99-1.12	0.1209
UP(≥ 0.5g/d as ref.)	2.96	2.40-3.66	<0.0001	2.39	1.85-3.09	<.0001
Hematuria score(≥ 3 as ref.)	0.93	0.75-1.15	0.4975	0.86	0.69-1.08	0.1953
Duration from occurrence of disease until diagnosis	0.99	0.97-1.00	0.1241	0.99	0.98-1.02	0.9286
oxford M (0 as ref.)	0.80	0.57-1.08	0.1483	1.04	0.73-1.45	0.8240
oxford E (0 as ref.)	1.17	0.89-1.52	0.2559	1.25	0.93-1.66	0.1390
oxford S (0 as ref.)	0.65	0.53-0.80	<0.0001	0.82	0.66-1.03	0.0842
oxford T(0 as ref.)	0.42	0.30-0.58	<0.0001	0.69	0.46-1.00	0.0545
PSL (yes)	0.87	0.68-1.10	0.2580	1.52	1.13-2.04	0.0066
RASI (yes)	0.41	0.32-0.51	<0.0001	0.39	0.30-0.51	<.0001
Anti-platelet agent (yes)	0.52	0.42-0.65	<0.0001	0.79	0.62-1.01	0.0552
Tonsillectomy (yes)	2.04	1.01-3.63	0.0456	0.99	0.45-1.94	0.9763

Factors associated with CR

	univariate analysis			multivariate analysis		
	HR	95%CI	p value	HR	95%CI	p value
gender(male1)	0.90	0.71-1.15	0.4168	1.01	0.77-1.31	0.9587
age(every 10y)	1.05	0.97-1.15	0.2420	1.28	1.13-1.43	<0.0001
MAP(every 10mmHg)	0.95	0.87-1.04	0.2715	1.06	0.95-1.19	0.3034
eGFR(every 10ml/min/1.73m^2)	1.04	0.99-1.09	0.0722	1.03	0.95-1.11	0.4778
UP(≥ 0.5g/d as ref.)	2.03	1.59-2.59	<0.0001	1.49	1.11-2.02	0.0082
Hematuria score (≥ 3 as ref.)	1.20	0.93-1.54	0.1593	1.13	0.86-1.47	0.3845
Duration from occurrence of disease until diagnosis	1.00	0.98-1.02	0.9823	1.00	0.98-1.02	0.9545
oxford M (0 as ref.)	0.84	0.57-1.20	0.3556	1.02	0.67-1.51	0.9088
oxford E (0 as ref.)	1.03	0.73-1.40	0.8776	1.13	0.79-1.59	0.4897
oxford S (0 as ref.)	0.71	0.56-0.90	0.0054	0.85	0.66-1.11	0.2396
oxford T(0 as ref.)	0.51	0.34-0.74	0.0002	0.61	0.38-0.93	0.0227
PSL (yes)	0.95	0.72-1.24	0.7135	1.54	1.10-2.13	0.0121
RASI (yes)	0.44	0.34-0.57	<0.0001	0.37	0.27-0.50	<.0001
Anti-platelet agents (yes)	0.50	0.39-0.65	<0.0001	0.71	0.53-0.95	0.021
Tonsillectomy (yes)	3.12	1.60-5.44	0.0017	2.32	1.05-4.54	0.0387

Maintain of remission
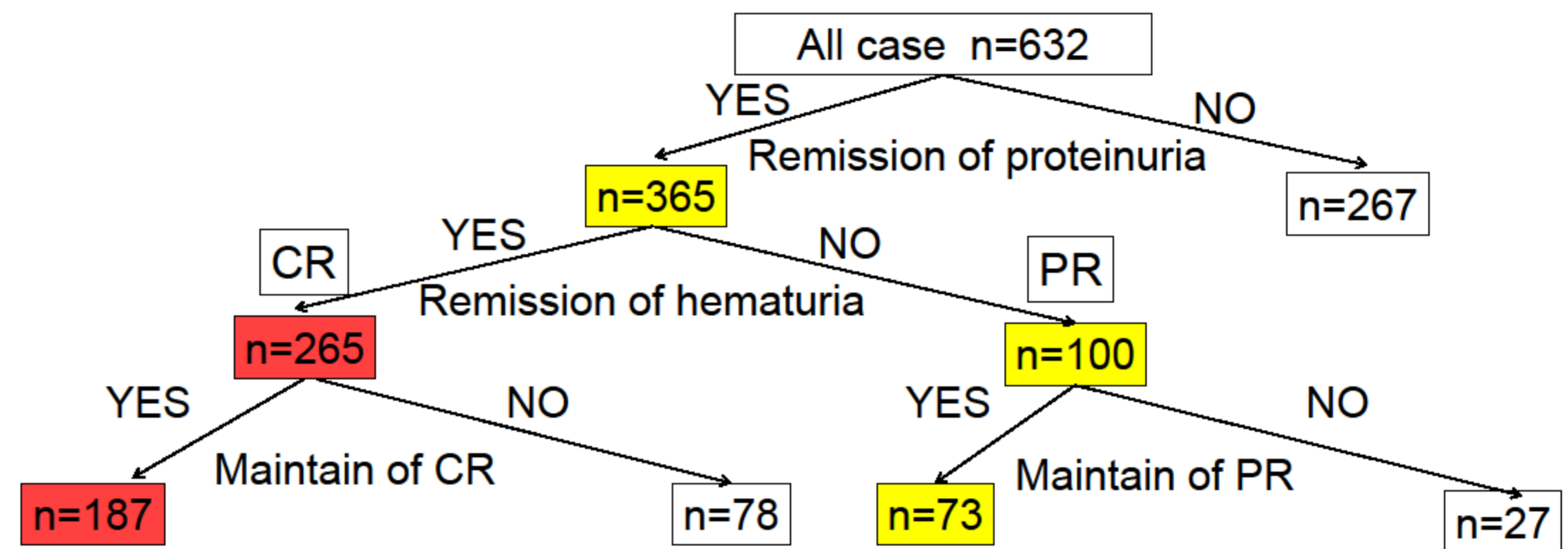
Event (50% decrease in eGFR)-free renal survival curve
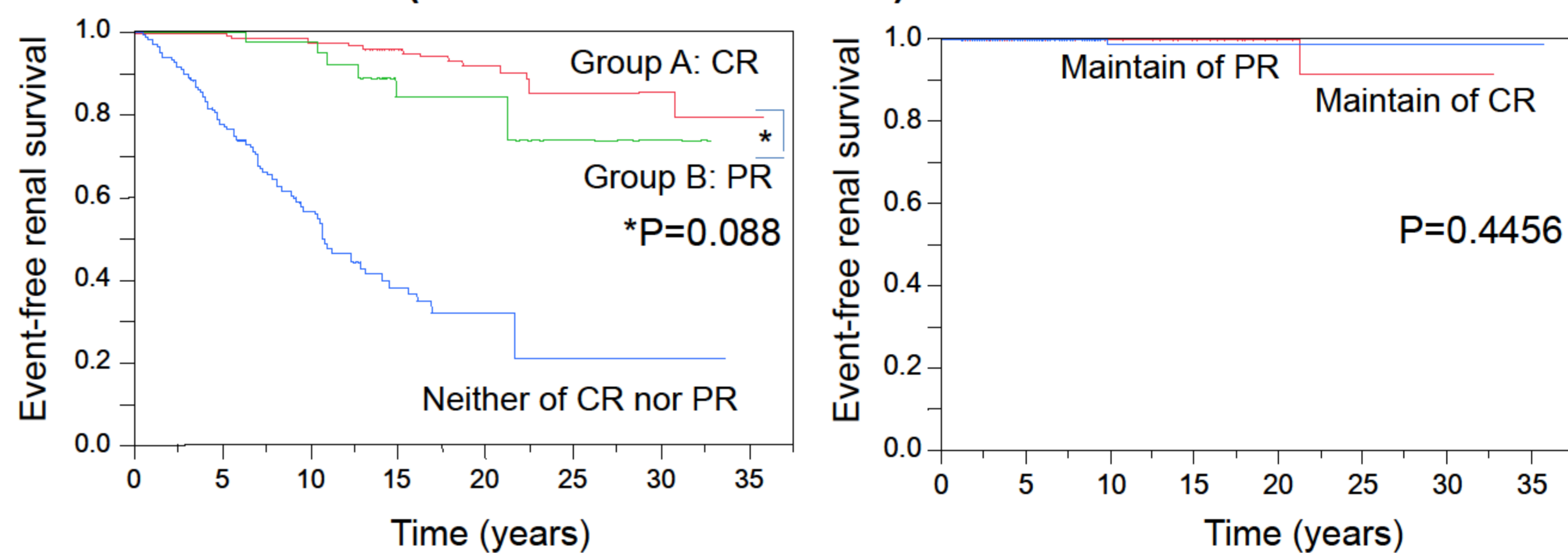
Summary and discussion

● The mean duration of follow-up was 11 years. Proteinuria remitted in 365 patients, and both proteinuria and hematuria remitted in 265 of them.
● Regarding factors associated with the remission of proteinuria, HR of urinary protein below 0.5 g/day was 2.39 (95% CI: 1.85-3.09) and that of steroid treatment was 1.52 (95% CI: 1.13-2.04).
● Regarding factors associated with the remission of both proteinuria and hematuria, in addition to urinary protein below 0.5 g/day and steroid treatment, the Oxford classification T score=0 (HR: 1.65, 95% CI:1.07-2.61) and tonsillectomy (HR: 2.32, 95% CI: 1.04-4.54) were significant factors.
● Only one patient each reached 50% reduction of eGFR out of the 73 and 187 patients who could maintain remission of PR and CR, respectively, showing that renal prognosis was favorable.
● These results suggest that mild proteinuria and mild histlogical findings , PSL treatment and tonsillectomy contribute to remission of IgA nephropathy.
● Proposal of remission criteria for IgA nephropathy in our country was thought to be useful, but achievement of CR was not indispensable for long-term renal prognosis.

Conclusion

These results suggest that long-term renal prognosis is favorable even when the remission of only proteinuria can be maintained, and the remission of hematuria may be unnecessary.

References

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