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A scoring system to predict renal outcome in IgA nephropathy: a nationwide 10-year prospective cohort study

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Abstract

Background. Immunoglobulin A nephropathy (IgAN) is the most common form of glomerulonephritis, and a substantial number of patients succumb to end-stage renal disease (ESRD). However, prediction of the renal outcome in individual patients remains difficult. We have already published a scoring system using the data in a prospective cohort of IgAN patients followed up from 1995 to 2002.

Methods. The cohort was further followed up until 2005 in 97 clinical units in Japan. The data from 2283 patients were analysed by Cox regression to determine the predictors of ESRD in IgAN, and their β-coefficients were converted into scores to estimate ESRD risk within 10 years.

Results. During the follow-up (median, 87 months), 252 patients developed ESRD. Male sex, age less than 30 years, family histories of chronic renal failure and chronic glomerulonephritis, hypertension, proteinuria, mild haematuria, hypoalbuminaemia, low glomerular filtration rate and a high histological grade at initial renal biopsy were associated with the risk of ESRD in the multivariable analysis. A scoring system was framed to estimate the 10-year ESRD risk using eight variables significant in both univariable and multivariable models. This prognostic score accurately classified patients by risk: patients with estimates of 0–4.9, 5.0–19.9, 20.0–49.9 and 50.0–100% had an observed incidence of 1.7, 8.3, 36.7 and 85.5%, respectively. The corresponding area under the receiver-operating characteristic curve was 0.942 (95% confidence interval, 0.925–0.958).

Conclusion. This validated scoring system to quantitatively estimate ESRD risk during the 10-year follow-up of IgAN patients will serve as a useful prognostic tool in clinical practice.

Keywords: cohort studies; IgA nephropathy; prognosis; renal dialysis; risk factors

Introduction

Immunoglobulin A nephropathy (IgAN) was described as a new clinical entity in 1968 by Berger and Hinglais [1], and is now the most common cause of idiopathic glomerulonephritis [2–4]. Long-term outcomes and prognostic factors of patients with IgAN have been evaluated in many studies. Although this disorder is thought to follow a benign course, many patients are at a risk of at least slow progression. Furthermore, end-stage renal disease (ESRD) developed in ∼15% of cases within 10 years [5].

Several tools have been available to estimate the renal prognosis using various clinical and pathological factors [6–9]. However, one was based on a relatively small size cohort [6], another used surrogate endpoints such as an increase in serum creatinine [7] and the others did not provide quantitative estimates of the ESRD risks [8,9].

We earlier proposed a valid scoring system to quantitatively predict renal outcomes based on the 7-year follow-up data involving more than 2000 patients with biopsy-proven IgAN [10]. However, renal function deteriorates so slowly in the early stage of IgAN that the longer the follow-up period, the more useful in the clinical settings is the constructed prediction model [7]. We, therefore, extended the follow-up of this cohort for 3 more years and refined the scoring system to predict renal outcomes at 10 years.

Methods

The details of the methods used here were described in our earlier 7-year follow-up study [10]. Briefly, 2450 patients with biopsy-proven IgAN from 97 clinical units were followed up from 1995 when a nationwide survey on IgAN was jointly conducted by the two research committees for the specified intractable diseases organized by the Japanese Government. Follow-up mail surveys to collect information on outcomes such as death, ESRD and serum creatinine were performed in 1997, 1999 and 2002 with response rates of 82.5, 95.7 and 93.3%, respectively. An additional survey was carried out in 2005 (response rate, 82.7%).

The baseline data of the patients were obtained by reviewing medical records in the nationwide survey in 1995. The data included sex, age, family history of chronic renal failure and chronic glomerulonephritis, initial clinical manifestations, year of diagnostic renal biopsy, systolic

Table 1. Criteria for histological grading from the Joint Committee of the Research Group on Progressive Renal Disease (Ministry of Health and Welfare of Japan) and the Japanese Society of Nephrology [12]

Grade	Glomerular findings	Interstitial and vascular findings
I	Slight mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to Bowman's capsule is not observed.	Prominent changes are not seen in the interstitium, renal tubuli or blood vessels.
II	Slight mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to Bowman's capsule seen in <10% of all biopsied glomeruli.	Same as above.
III	Moderate, diffuse mesangial cell proliferation and increased matrix. Glomerulosclerosis crescent formation or adhesion to Bowman's capsule seen in 10–30% of all biopsied glomeruli.	Cellular infiltration is slight in the interstitium except around some sclerosed glomeruli. Tubular atrophy is slight, and mild vascular sclerosis is observed.
IV	Severe, diffuse mesangial cell proliferation and increased matrix. Glomerulosclerosis, crescent formation or adhesion to Bowman's capsule seen in >30% of all biopsied glomeruli. When sites of sclerosis are totalled and converted to global sclerosis, the sclerosis rate is >50% of all glomeruli. Some glomeruli also show compensatory hypertrophy. The sclerosis rate is the most important of these indices.	Interstitial cellular infiltration and tubular atrophy, as well as fibrosis are seen. Hyperplasia or degeneration may be seen in some intrarenal arteriolar walls.

and diastolic blood pressure, urine protein and blood, serum total protein and albumin and serum creatinine. Proteinuria was semiquantified with a standard urine dipstick with (−), (±), (+), (++) and (+++) corresponding to <10, 10–29, 30–99, 100–299 and ≥300 mg/dL of urine albumin, respectively. For estimation of the glomerular filtration rate (GFR), the estimation equation for Japanese patients with chronic kidney disease was applied [11]. This equation calculates the GFR from serum creatinine, age and gender. Histological grade at initial renal biopsy was assessed using the criteria from the joint committee of one of the aforementioned governmental research committees and the Japanese Society of Nephrology (Table 1) [12]. Information on therapy was collected in 1997, 2 years after the beginning of the follow-up.

Statistical methods

The study endpoint was ESRD defined as the initiation of chronic haemodialysis. Since there was little influence of competing risks in the current study, the complement of a Kaplan–Meier survival estimate was referred to as the 10-year cumulative incidence (risk) of ESRD [13]. Hazard ratios of potential prognostic factors were estimated using the Cox proportional hazards regression model. The independent effect of each variable was assessed by multivariable analysis. Systolic or diastolic blood pressure and serum total protein or albumin were included in the multivariable model because of their close relationship with each other. Akaike's Information Criterion (AIC) and the Bayesian Information Criterion (BIC) were used to select the most appropriate covariance structure.

Development of the scoring system

A scoring system to predict ESRD in individual patients with IgAN was composed based on the proportional hazards model including the significant variables in the aforementioned multivariable analysis. To enhance parsimony, only variables that possessed significant univariate relationships with ESRD were included in the final scoring system [14]. To generate a simple integer-based point score for each predictor variable, scores were given by multiplying the β-coefficient by 10 and rounding up or down to the nearest integer. The overall risk score for each patient was calculated by summing the scores of all components. The baseline survivor function was estimated by the Kaplan–Meier product–limit estimate.

Evaluation of the scoring system

To examine the goodness of fit of the scoring system to the data, we divided the patients into four groups according to the predicted 10-year risk of ESRD, that is, low (0–4.9%), moderate (5.0–19.9%), high (20.0–49.9%) and very high (50.0–100%). The renal survival curve of ESRD was then drawn in each group using the Kaplan–Meier method. To further assess the utility of the score, we used the area under the receiver-operating characteristic (ROC) curve for the 10-year risk of ESRD. The area and its 95% confidence interval (CI) were estimated by the nonparametric method.

As an additional analysis, one-third of the participants were randomly allocated to a validation sample and the remainder to a derivation sample. The prognostic score was developed in the derivation sample, and the actual 10-year cumulative incidence of ESRD was computed by the predicted risk in the validation sample. The area under the ROC curve was also estimated in the validation group. Considering the sampling error, we repeated this procedure in 100 different validation sets.

Statistical analyses were performed using the Stata 10.1 software (Stata Corporation, College Station, TX, USA). All tests of significance were two-tailed, and P-values <0.05 were considered statistically significant. This investigation was approved by the Ethics Committee of Kyoto University Graduate School of Medicine and the Ethics Committee of the Juntendo University School of Medicine.

Results

Participants' demographic and clinical characteristics

Out of the 2450 patients tracked from 1995, 165 patients with unknown outcomes and 2 patients with erroneous baseline serum creatinine levels were excluded, leaving 2283 patients in the current analysis. The median age of the included patients at baseline was 32.1 years [interquartile range (IQR), 20.7–46.9], and 51.3% were women. During the follow-up of 14 975 person-years [median follow-up period, 87 months (IQR, 42–122)], 252 patients (11.0%) developed ESRD. The renal survival rate at 10 years was 85.0% (95% CI, 83.1–86.7). Twenty-one deaths without ESRD were also reported: six from circulatory diseases, six from neoplasms, two from other causes and seven from unknown causes. By 1997, 34.5%, 10.6% and 28.2% of the patients had received corticosteroids, immunosuppressive agents and angiotensin-converting enzyme inhibitors (ACEi), respectively.

Table 2 summarizes the 10-year cumulative incidence of ESRD by demographic and clinical factors and their hazard

Table 2. Ten-year cumulative incidence of end-stage renal disease by baseline demographic and clinical characteristics and their hazard ratio

				10-year cumulative incidence of ESRD		Hazard ratio for ESRD		
	n	Observed person-years	No. of ESRD	%	95% CI	Hazard ratio	95% CI	*P*-value
Sex								
Women	1171	7926	94	11.1	9.1–13.5	1.00	–	
Men	1112	7049	158	19.3	16.6–22.3	1.88	1.46–2.43	<0.001
Age (years)								
∼19	530	3089	13	4.4	2.4–8.0	1.00	–	
20–29	508	3195	39	10.9	8.0–14.8	2.94	1.57–5.50	
30–39	368	2580	39	13.4	9.8–18.2	3.69	1.97–6.91	
40–49	458	3330	75	20.2	16.4–24.8	5.53	3.07–9.98	
50–59	288	1947	58	24.1	19.0–30.2	7.25	3.97–13.2	
60 and above	131	834	28	26.6	18.9–36.8	8.09	4.19–15.6	<0.001 for trend
Family history of chronic renal failure								
No	2189	14 393	239	15.0	13.2–16.9	1.00	–	
Yes	94	582	13	16.5	9.6–27.6	1.34	0.77–2.35	0.30
Family history of chronic glomerulonephritis								
No	2146	14 113	236	15.0	13.3–17.0	1.00	–	
Yes	137	862	16	15.1	9.2–24.1	1.11	0.67–1.83	0.70
Initial manifestation								
By chance in a health check-up	1588	10 400	185	15.5	13.5–17.8	1.00	–	
Macrohaematuria	260	1747	14	8.7	5.0–14.7	0.45	0.26–0.77	0.004
Acute nephritis	112	721	8	10.5	5.1–21.0	0.62	0.31–1.26	0.19
Nephrosis	66	421	11	24.4	13.9–40.5	1.46	0.79–2.68	0.23
Other	233	1536	33	19.1	13.7–26.2	1.21	0.83–1.75	0.32
Year of initial renal biopsy								
1994–1995	481	3130	43	13.8	10.2–18.5	1.00	–	
1992–1993	596	3847	62	13.9	10.9–17.7	1.18	0.80–1.74	
1990–1991	403	2551	47	15.3	11.5–20.2	1.34	0.89–2.03	
1988–1989	291	2057	35	16.1	11.6–22.2	1.25	0.80–1.95	
1987 or before	474	3110	63	17.5	13.8–22.0	1.49	1.01–2.19	0.049 for trend
Systolic blood pressure (mmHg)								
≤120	1037	6845	49	7.0	5.3–9.3	1.00	–	
121–130	437	2902	51	16.6	12.7–21.5	2.45	1.66–3.63	
131–140	311	2103	54	22.1	17.2–28.1	3.61	2.45–5.31	
141–150	175	1075	43	31.6	24.2–40.6	5.56	3.69–8.38	
151–160	77	494	17	24.0	15.2–36.6	4.83	2.78–8.38	
>160	47	280	16	37.4	24.5–54.2	8.03	4.57–14.1	<0.001 for trend
Diastolic blood pressure (mmHg)								
≤70	961	6225	43	6.7	4.9–9.1	1.00	–	
71–80	549	3703	65	16.5	13.1–20.7	2.56	1.74–3.76	
81–90	396	2591	82	25.3	20.7–30.7	4.60	3.18–6.65	
91–100	150	1019	33	26.1	19.2–35.0	4.74	3.01–7.46	
>100	28	160	7	32.4	16.5–57.5	6.28	2.83–14.0	<0.001 for trend
Urine protein								
(−), (±)	834	5369	6	1.3	0.6–3.1	1.00	–	
(+)	528	3719	30	8.1	5.6–11.5	7.28	3.03–17.5	
(++)	488	3208	88	23.2	19.0–28.0	24.6	10.8–56.4	
(+++)	333	2040	109	39.5	33.7–45.9	47.7	21.0–108.5	<0.001 for trend
Urine red blood cells (/high-power field)								
None	582	3631	27	7.8	5.3–11.5	1.00	–	
1–29	1244	8216	172	18.2	15.7–20.9	2.83	1.89–4.25	
≥30	366	2550	35	12.3	8.8–17.0	1.86	1.13–3.08	0.009 for trend
Serum total protein (g/dL)								
≥7.5	448	3020	14	4.8	2.8–8.1	1.00	–	
7.0–7.4	764	4999	57	11.2	8.6–14.5	2.45	1.36–4.39	
6.5–6.9	682	4632	81	15.6	12.6–19.2	3.77	2.14–6.65	
6.0–6.4	245	1513	61	31.2	24.9–38.7	8.60	4.81–15.4	
≤5.9	77	448	33	48.3	36.8–61.3	15.8	8.48–29.6	<0.001 for trend
Serum albumin (g/dL)								
≥4.4	826	5427	36	6.6	4.7–9.1	1.00	–	
4.2–4.3	437	2989	28	9.7	6.7–14.0	1.41	0.86–2.32	
4.0–4.1	362	2529	46	15.9	12.0–20.9	2.75	1.78–4.25	
3.8–3.9	229	1463	42	23.5	17.7–30.8	4.31	2.76–6.73	
≤3.7	229	1379	81	41.4	34.6–49.0	8.81	5.95–13.0	<0.001 for trend

Continued.

Table 2. *Continued.*

	n	Observed person-years	No. of ESRD	10-year cumulative incidence of ESRD		Hazard ratio for ESRD		
				%	95% CI	Hazard ratio	95% CI	*P*-value
GFR (mL/min/1.73 m^2)								
≥90	820	5087	11	2.6	1.4–4.7	1.00	–	
60–90	741	5330	23	4.8	3.2–7.2	1.95	0.95–4.01	
30–60	564	4018	94	21.4	17.7–25.7	10.6	5.70–19.9	
15–30	114	497	81	81.3	72.2–88.8	80.4	42.8–151.0	
<15	44	43	43	–[a]	–[a]	679.9	340.3–1358.3	<0.001 for trend
Histological grade at initial renal biopsy								
Grade I	517	3232	13	4.7	2.7–8.2	1.00	–	
Grade II	702	4805	29	6.2	4.3–9.0	1.51	0.79–2.91	
Grade III	693	4802	105	19.7	16.5–23.5	5.48	3.08–9.75	
Grade IV	212	1153	89	48.4	41.1–56.3	19.2	10.7–34.4	<0.001 for trend

ESRD, end-stage renal disease; CI, confidence interval; GFR, glomerular filtration rate.
[a]All patients reached ESRD or were censored before 120 months.

ratios. Male sex, advanced age, earlier renal biopsy, higher systolic and diastolic blood pressure, more severe proteinuria, lower serum total protein and albumin, lower GFR and higher histological grade were significantly associated with the risk of ESRD. On the other hand, patients whose initial clinical manifestation was macrohaematuria had favourable renal outcomes. Mild haematuria, 1–29 red blood cells per high-power field (RBCs/HPF), showed a higher risk than severe haematuria, ≥30 RBCs/HPF (18.2% versus 12.3%). There were no remarkable differences in risk between histological grade I and II (4.7% versus 6.2%).

Multivariable analysis and development of the scoring system

Results of the multivariable analysis for the risk of ESRD by factors are summarized in Table 3. Family histories of chronic renal failure and chronic glomerulonephritis were significant factors for predicting renal outcome in the multivariable model. Instead, initial manifestation of macrohaematuria and earlier renal biopsy were no longer significant. Male sex, higher systolic blood pressure, more severe proteinuria, mild haematuria, hypoalbuminaemia, lower GFR and higher histological grade were associated with the development of ESRD. Patients aged less than 30 years were at higher risk in the multivariable model, whereas an upward trend in the hazard ratio with advancing age was found in the univariate analysis.

Based on these analyses, we composed a scoring system to estimate a 10-year risk of ESRD. Because the presence of family histories of chronic renal failure and chronic glomerulonephritis had no significant univariate relationships with ESRD and the area under the ROC curve of the model was rather smaller than that without these variables, they were removed from the final prediction scheme. Table 4(a) lists the scores of individual prognostic factors. The sum of individual scores can then be converted into the corresponding estimated risk using those shown in Table 4(b). The baseline survivor function was estimated as 0.9993504 at 10 years.

Table 3. Hazard ratios of end-stage renal disease by major baseline demographic and clinical factors using multivariable analysis

	Hazard ratio	95% CI	*P*-value
Male sex	1.73	1.25–2.38	0.001
Age <30 years	3.41	2.13–5.46	<0.001
Family history of chronic renal failure	2.49	1.20–5.17	0.015
Family history of chronic glomerulonephritis	2.07	1.07–4.02	0.031
Systolic blood pressure (mmHg)			
≤130	1.00	–	–
131–160	1.46	1.06–2.00	0.020
>160	3.13	1.63–6.03	0.001
Urine protein			
(−), (±)	1.00	–	–
(+)	3.41	1.29–9.06	0.014
(++)	8.12	3.22–20.5	<0.001
(+++)	12.4	4.91–31.3	<0.001
Mild haematuria (1–29 RBC/HPF)	2.34	1.64–3.33	<0.001
Serum albumin <4.0 g/dL	1.94	1.41–2.66	<0.001
Glomerular filtration rate (mL/min/1.73 m^2)			
≥90	1.00	–	–
60–90	2.31	0.98–5.41	0.055
30–60	9.46	4.12–21.7	<0.001
15–30	76.2	31.6–183.7	<0.001
<15	880.3	326.9–2370.5	<0.001
Histological grade III or IV at initial renal biopsy	1.70	1.12–2.56	0.012

CI, confidence interval; RBC/HPF, red blood cells per high-power field.

Evaluation of the scoring system

The renal survival curves according to the estimated 10-year risk are shown in Figure 1. The prognostic score successfully classified the patients by risk. Those with an

Table 4. Scores to estimate the risk of end-stage renal disease (ESRD) by demographic and clinical factors (a) and the estimated 10-year risk of ESRD by total score (b)

(a) Scores of individual prognostic factors

	Score
Male sex	6
Age <30 years	12
Systolic blood pressure (mmHg)	
≤130	0
131–160	4
>160	11
Urine protein	
(−), (±)	0
(+)	12
(++)	21
(+++)	25
Mild haematuria (1–29 RBC/HPF)	8
Serum albumin <4.0 g/dL	7
Glomerular filtration rate (mL/min/1.73 m^2)	
≥90	0
60–90	7
30–60	22
15–30	42
<15	66
Histological grade III or IV	5

(b) Estimated 10-year risk of ESRD by total score

Total score	Estimated 10-year risk of ESRD (%)
0–26	0–1
27–43	1–5
44–50	5–10
51–58	10–20
59–63	20–30
64–70	30–50
71–75	50–70
76–82	70–90
83–140	90–100

RBC/HPF, red blood cells per high-power field.

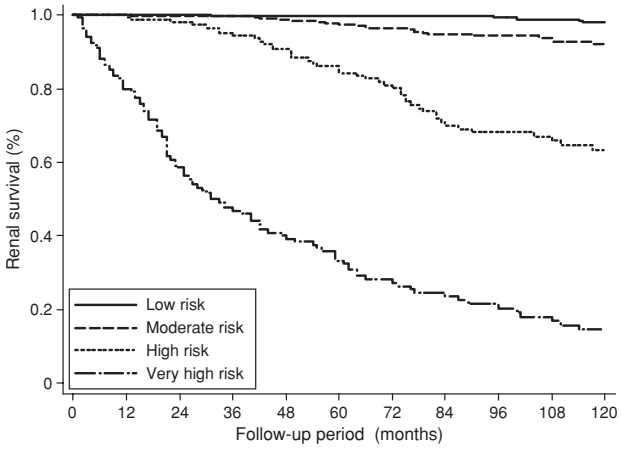

Fig. 1. Renal survival curves by estimated 10-year risk of end-stage renal disease. Patients were categorized into four groups according to the estimated risk: low (0–4.9%, $n = 1007$), moderate (5.0–19.9%, $n = 365$), high (20.0–49.9%, $n = 154$) and very high (50.0–100%, $n = 135$). Numbers of patients at risk were 1661, 1430, 1216, 1005, 706 and 537 at 0, 2, 4, 6, 8 and 10 years, respectively.

estimated risk of 0–4.9% (score, 0–43), 5.0–19.9% (44–58), 20.0–49.9% (59–70) and 50.0–100% (71 or more) had an actual cumulative incidence of ESRD in 10 years of 1.7% (95% CI, 0.86–3.5), 8.3% (5.4–12.5), 36.7% (28.4–46.5) and 85.5% (78.0–91.5), respectively. This indicated a good agreement between the estimated and observed risks. Furthermore, the area under the ROC curve of this prediction model reached 0.942 (95% CI, 0.925–0.958) (Figure 2).

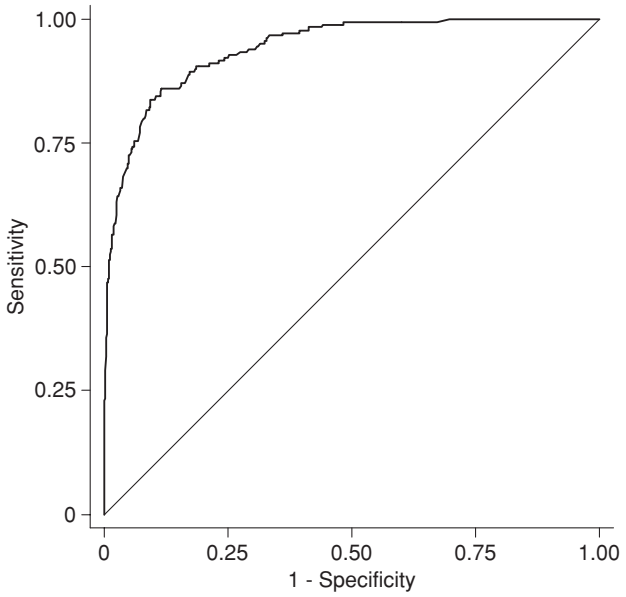

Fig. 2. The receiver-operating characteristic curve for predicting end-stage renal disease within 10 years by current scoring system.

Even when the prognostic scores were developed using derivation samples randomly selected from all participants, the estimated 10-year cumulative incidence of ESRD well predicted the observed ones in the remaining validation sample. The median values of observed 10-year incidence were 2.2% (IQR, 1.5–3.0%), 9.2% (7.4–11.8), 34.3% (30.4–38.6) and 83.4% (76.7–87.1) in patients with an estimated risk of 0–4.9, 5.0–19.9, 20.0–49.9 and 50.0–100%, respectively. The median of the corresponding area under the ROC curve (0.935; IQR, 0.924–0.944) was comparable with the area in the full dataset (0.942).

Discussion

Based on a large-scale cohort study, we described the prognostic indicators for IgAN and developed a scoring system for estimating the ESRD risk within 10 years. Male sex, age less than 30 years, the presence of family histories of chronic renal failure and chronic glomerulonephritis, higher systolic blood pressure, more severe proteinuria, mild haematuria, hypoalbuminaemia, lower GFR and higher histological grade were related to the risk. The prognostic score comprising eight variables significant in both univariable and multivariable models successfully classified patients according to their ESRD risk, and the accuracy in predicting the ESRD was excellent.

We could establish a much simpler scoring system than the former one based on the 7-year follow-up data [10] by reducing the number of choices of each scoring item. Nevertheless, we did not compromise with the predictability; the areas under the ROC curve estimating ESRD risk rather increased by 0.003 from 0.939 (95% CI, 0.921–0.958) [10].

Male sex was a significant risk factor for ESRD in the current model, whereas it made a favourable contribution in

the former scoring. It would be attributable to the overestimation of the women's kidney function based only on serum creatinine in our previous analysis. We could estimate GFR more elaborately based on serum creatinine, as well as age and gender in the current analysis, which made our understanding of the relationships between each predictor much simpler. One of the reasons for the increase in the relative weight of the age variable in the current model compared to that in the previous one is also this overestimation of the baseline renal function among the older patients. Contrary to the age variable, the prognostic value of the histological grade at initial renal biopsy declined by extending the follow-up period.

We selected serum albumin in the current multivariable model, instead of serum total protein in the prior one, because both AIC and BIC of the model were substantially decreased by replacing serum total protein with serum albumin. This replacement seems rational from the pathophysiological viewpoint that glomerular proteinuria is mainly composed of albumin.

In the multivariable analysis, we found that the presence of family histories of chronic renal failure and chronic glomerulonephritis were associated with the development of ESRD. Several genetic factors are considered to be associated with the prognosis of IgAN. For example, some genes related to the renin–angiotensin system are suggested to have prognostical importance [15–17]. A report from China suggested an association between the polymorphism of the megsin gene, a kidney-specific serine protease inhibitor, and the progression of IgAN [18]. Furthermore, familial IgAN was reported to have a worse prognosis in an observational epidemiological study [19]. Nevertheless, the influences of genetic inheritance are still in controversy and have not reached a consensus [16,20–22].

In virtue of the current scoring system, clinicians can quantitatively estimate ESRD risks during 10 years of follow-up of IgAN patients by summing up only eight integers yielded from the routine clinico-pathological data. The validated, multivariable regression-based model should aid medical decision making about patients with biopsy-proved IgAN. Patients judged to be at higher risk can receive more frequent monitoring and more intensive treatment, whereas patients estimated to be at lower risk can be reassured and given less intensive care.

Given the nature of the observational design and the insufficient information regarding treatment, a clear evaluation of the influence of therapy is beyond the scope of the current analysis. Even though the optimal approach to the treatment of IgAN is uncertain, some strategies have been proved effective in reducing proteinuria and the rate of disease progression through the accumulation of evidence during the last decade. According to both observational studies [23,24] and randomized trials [25–27], ACEi and angiotensin II receptor blockers have a definite role in treating IgAN, particularly of the hypertensive and proteinuric forms. A review supports the use of corticosteroids and other immunosuppressive agents in reducing proteinuria or preventing progression to ESRD [28]. Increasing attention has been paid to the role of tonsillectomy for the long-term prognosis of IgAN [29,30]. The estimated risk of ESRD by the current scoring system, therefore, might be attenuated for patients properly treated in the latter portion of the observation interval.

Some other potential limitations of the current analysis must be acknowledged. First, because the data on 24-h urinary protein excretion were not available for two-thirds of the patients and those on urinary creatinine were not collected, we had to assess proteinuria with simple dipstick urine test results. However, the semiquantified proteinuria was reproducible and considerably correlated with the 24-h urinary excretion of protein [10,31], and the predictability of the current scoring system was excellent. Feasibility in clinical settings would override theoretical propriety. From a pragmatic standpoint, clinicians should average or take the median of the results of several urinalyses when applying this scoring system. Second, the current scoring system was developed among Japanese patients, and the applicability of the results to other races was not verified. Another study adjusting for racial differences in serum creatinine, which was a main determinant of GFR in the estimation equation, would assure the generalizability of the current scoring system.

In summary, the present study revealed that male sex, age less than 30 years, family histories of chronic renal failure and chronic glomerulonephritis, hypertension, proteinuria, mild haematuria, hypoalbuminaemia, low GFR and advanced histological changes increased the risk of ESRD in IgAN patients. The ESRD prediction score based on a multivariable model was sufficiently valid and will serve as a useful tool for clinicians treating IgAN patients.

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Conflict of interest statement. Seven-year follow-up data from this cohort have already been published in Nephrology Dialysis Transplantation, October, 2006. The authors declare no conflict of interest.

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Plasma markers of coagulation and endothelial activation in Fabry disease: impact of renal impairment*

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Abstract

Background. In Fabry disease, storage of globotriaosylceramide (Gb3) in arterial walls is one of the main pathogenetic factors that are thought to underlie the clinical manifestations of the disease. Abnormalities of the vessel wall, haemodynamics and pro- and anticoagulant factors may play a role, though the exact pathophysiology is incompletely understood. In this study, we try to clarify