

# PROGNOSTIC RISK FACTORS FOR IDIOPATHIC MEMBRANOUS NEPHROPATHY

Noriko Hayami, Yoshifumi Ubara, Junichi Hoshino  
Department of Nephrology, Toranomom Hospital, Japan.

## BACKGROUND

Membranous nephropathy (MN) is a common cause of the nephrotic syndrome in adults. Idiopathic membranous nephropathy (IMN) has a favorable outcome in most patients, but some reports show that 30-40% of patients slowly progress to end-stage renal disease (ESRD).

M-type phospholipase A2 receptor (PLA2R) is identified as major antigen in idiopathic MN. It is reported that anti-PLA2R antibodies are associated with renal outcome. But the prevalence of anti-PLA2R antibodies varies by countries. In Japan, the prevalence of anti-PLA2R antibodies is about 50% and it is lower than in other countries. It is unclear whether anti-PLA2R antibodies are associated with renal outcome in Japan.

## OBJECTIVES

This study aimed to evaluate clinicopathological features of IMN and determine whether anti-PLA2R antibodies are associated with renal outcome.

## METHODS

285 patients who diagnosed with IMN by renal biopsy from 1988 to 2015 at Toranomom Hospital were enrolled in this study. We excluded 128 patients with secondary MN that have apparent cause of MN, such as collagen disease, hepatitis, bucillamine use or cancer. Anti-PLA2R antibodies were measured by enzyme-linked immunosorbent assay (ELISA), and it is performed before patients were treated. Results of immunofluorescent staining for IgG subclass were converted (-) into 0, (+) into 1 and (2+) into 2. Complete remission was defined as proteinuria of less than 0.3g/day. Kaplan-Meier survival analysis was performed with the endpoint of need for dialysis or doubling of serum creatinine. Multivariate analyses were performed using the Cox proportional hazards regression model to identify the significant variables for predicting renal survival.

## RESULTS

	n=157
Age at renal biopsy, yr	60 (52-69)
Male gender, n (%)	108 (69)
Serum Creatinine, mg/dl	0.9 (0.7-1.1)
eGFR, ml/min/1.73m <sup>2</sup>	66 (51-78)
Serum albumin, g/dl	3.0 (2.0-4.0)
Anti-PLA2R antibody, %	37
Proteinuria, g/day	2.4 (1.0-4.5)
Nephrotic syndrome, n (%)	124 (46)
Use of immunosuppressant, n (%)	107 (68)
Follow-up, yr	7.3 (3.9-14.1)

Table1. Characteristics of IMN patients.

[median (IQR)]

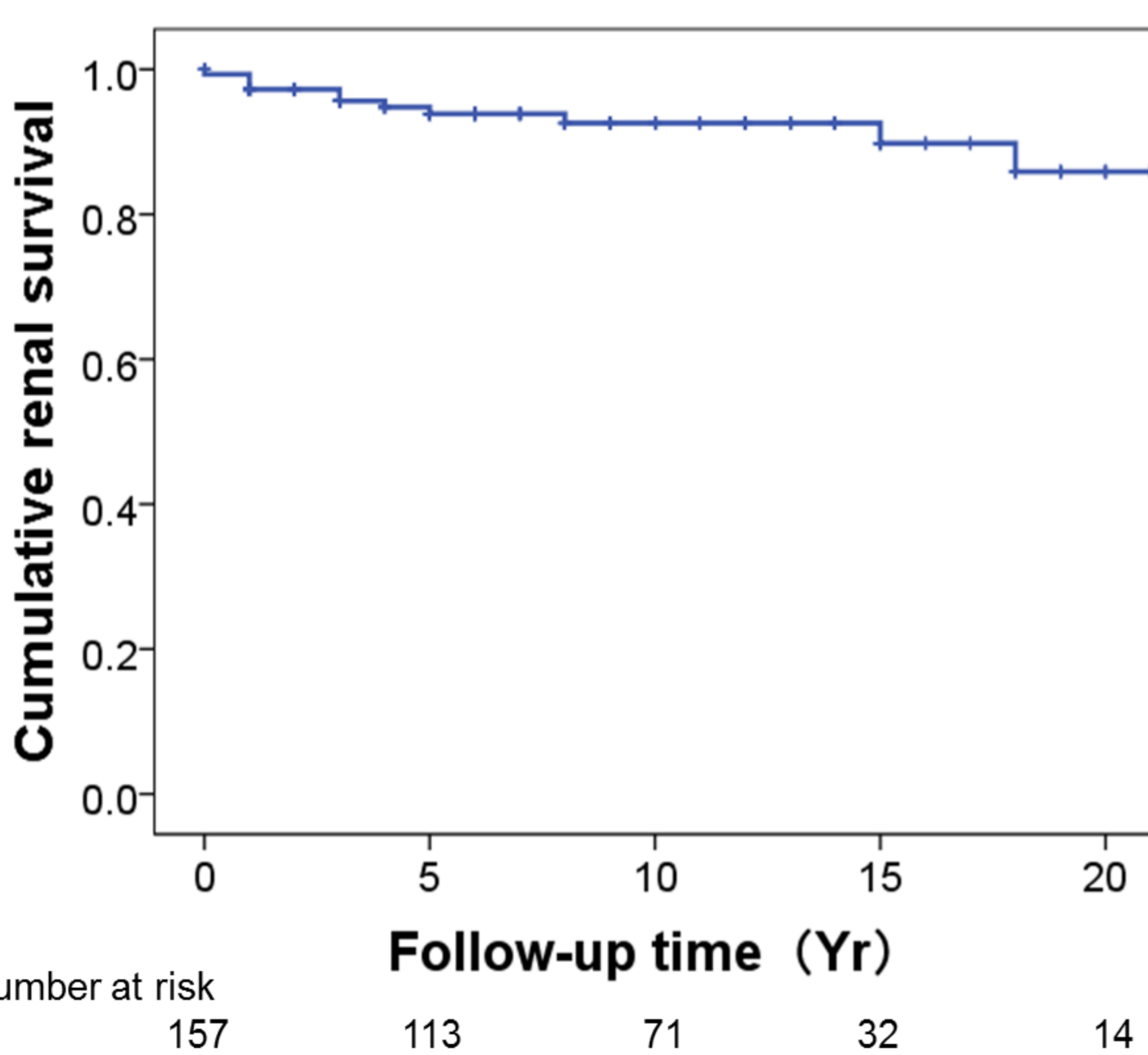


Fig. 1. Kaplan-Meier curves for renal survival  
5-year and 10-year renal survival were 93.9% and 92.6%.

	n=157
FGS lesion	13 (8.4%)
Interstitial fibrosis / tubular atrophy (IFTA)	57 (38%)
	0%
	1-25%
	25-49%
	50%-
	3 (2%)
IgG subclass (mean ±SD)	
	IgG1
	1.1 ± 0.7
	IgG2
	0.4 ± 0.5
	IgG3
	0.5 ± 0.5
	IgG4
	1.8 ± 0.4
Stage	
	I
	68 (27%)
	II
	114 (46%)
	III
	63 (25%)
	IV
	3 (1%)

Table2. Findings of Renal biopsy

Variable	Univariate			Multivariate		
	HR	0.95% CI	p value	HR	0.95% CI	p value
Gender, male	1.23	0.33 – 4.65	0.76	1.15	0.23 - 1.60	0.87
Age at biopsy	1.09	1.02 – 1.17	0.02	1.11	0.90 – 1.00	0.05
<b>Serum Creatinine</b>	<b>6.72</b>	<b>3.17 – 14.3</b>	<b>&lt;0.01*</b>	<b>6.25</b>	<b>2.24 – 17.4</b>	<b>&lt;0.01*</b>
Anti-PLA2R antibody	4.90	0.81 - 29.3	0.07	3.25	0.78 – 15.2	0.10
Proteinuria	1.18	0.99 – 1.38	0.05	1.09	0.87 - 1.34	0.45
Immunosuppressant	1.71	0.37-7.93	0.49	1.23	0.21 – 7.37	0.82
Complete remission	0.16	0.05 – 0.57	<0.01*	0.36	0.09 – 1.56	0.17

Table3. Univariate and multivariate analysis of risk factors for renal outcome. (\* p<0.05)

Anti-PLA2R antibodies were positive in only 37% of IMN patients. Serum Creatinine was associated with renal outcome.

## CONCLUSIONS

The prevalence of Anti-PLA2R antibodies was lower than that of previous studies. Anti-PLA2R antibodies were not significant factor associated with renal outcome.