The Association Between Variants in PLA2R and HLA-DQA1 and Renal Outcomes in Patients With Primary Membranous Nephropathy in Western China

Shulei Fan

Nephrology

Qiuxia Wang

Nephrology

Amanda Y Wang

Nephrology

Ping Zhang

Nephrology

Xiang Zhong

Nephrology

Shasha Chen

Nephrology

Guisen Li

Nephrology

Li Wang

Nephrology

Wei Wang (✉ wwei958@163.com)

Nephrology <https://orcid.org/0000-0001-5664-7725>

Research article

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Abstract

Background Both Genome-wide associations and our previous study have shown that single nucleotide polymorphisms (SNPs) of M-type phospholipase A2 receptor (PLA2R) and human leukocyte antigen complex class II HLA-DQ α -chain 1 (HLA-DQA1) gene were identified to be associated with primary membranous nephropathy (PMN). However, whether these SNPs affect clinical manifestation and renal outcome for PMN patients is poorly defined. Here, we evaluated whether there is an association between these SNPs and clinical manifestations and renal outcomes of PMN in a western Chinese cohort.

Methods: Seven SNPs within PLA2R and one SNP in HLA-DQA1 were selected in our study. Clinical data from 314 patients with PMN were collected and the relationship between the genotype and phenotype was evaluated. A total of 186 patients had follow-up data. We assessed the treatment responses and renal outcomes between patients with these gene polymorphisms after a median follow-up of 18.6 months.

Results: Eight SNPs were not associated clinical manifestations of PMN patients ($P < 0.05$). rs3828323 T allele was marginally significantly associated with hypertension ($P = 0.008$, $P_c = 0.064$, OR = 1.821). After treatment for PMN, urea (OR = 1.184, 95%CI: 1.030-1.361, $P = 0.017$) was a risk factor for non-remission of the disease, eGFR (OR = 0.984, 95%CI: 0.970-0.998, $P = 0.028$) and albumin (OR = 0.922, 95%CI: 0.880-0.966, $P = 0.001$) were protective factors for non-remission of the disease. We also identified that PMN patients with CT/TT genotype for rs3828323 achieved higher cumulative survival rate than patients with CC genotype.

Conclusions Rs3828323 may influence hypertension and renal outcome in patients with PMN. Further research is needed to explore the mechanism for this genotype-disease phenotype association.

Background

Primary membranous nephropathy (PMN) is one of the most common causes for nephrotic syndrome for adult. Its typical pathological features are diffuse thickening of glomerular capillary basement membrane and deposition of subepithelial immune complexes[1, 2]. In recent years, its incidence is increasing. It is the second most common type of primary glomerulonephritis in China[3, 4].

PMN is a typical kidney disease caused by antigen-antibody reaction. Antigen-antibody binding forms immune complex, then activates complement system, resulting in injury of podocytes and glomerular basement membrane, and eventually leading to kidney injury[5, 6]. The production of circulating PLA2R antibodies may be the main pathogenic mechanism of the disease[7]. The anti-PLA2R antibody has high specificity and good sensitivity. 70% to 80% of PMN patients are PLA2R positive. The higher the antibody titer is, the higher the risk of deterioration of renal function is [8, 9]. It is reported that some clinical factors are related to the progress of the disease, including severe proteinuria, hypertension, and renal dysfunction at diagnosis[10, 11].

In Caucasian population, genome-wide association studies have confirmed the susceptibility of PLA2R and HLA-DQA1 gene with PMN[12]. Multiple loci in PLA2R and HLA-DQA1 were closely related to PMN in various ethnicities, but the results of different regions and ethnic groups were not entirely consistent [12-18]. To verify the previous findings in Western China, in our previous study we selected eight SNPs reported in the literatures and found that two SNPs (rs2715918, rs4665143) within PLA2R, 1 SNP in HLA-DQA1 (rs2187668) were associated with primary membranous nephropathy[19]. The interactions of rs2715918, rs4665143 and rs2187668 were associated with an increased risk of the development of PMN by 10.61-fold. Patients carrying risk alleles confer a predisposition to anti-PLA2R autoantibody generation[19]. In a Spanish study, Bullich et al found that PMN patients with two SNP risk alleles, rs2187668 and rs4664308, had better response to immunosuppressive therapy and slower progression of chronic kidney disease[17]. Wang et al found that PMN Patients with HLA-DRB1*1502 had worse kidney outcomes in Han Chinese[20].

To evaluate whether these SNPs are associated with clinical manifestations and renal outcomes of PMN patients, clinical data from 314 patients with PMN were collected and the relationship between the genotype and phenotype was evaluated. We performed a retrospective cohort study of 186 patients who had follow-up data to assess the relationship between genetic polymorphisms and renal outcome.

Methods

Patients

From January 2010 to December 2016, patients with biopsy-proven PMN in Sichuan Provincial People's Hospital were recruited. Among them, 314 patients who had complete clinical baseline data in our Renal Treatment System (RTS) database were included in the study. All the patients came from Western Han ethnicity. In addition, the data on complete follow-up more than 3 months were available and recorded in 186 patients. Patients with membranous nephropathy due to secondary causes, such as systemic lupus erythematosus, cancer, hepatitis B virus infection and drug were excluded.

The study was approved by the Ethics Committee of the Sichuan Provincial People's Hospital (Chengdu, China), and all the patients signed informed consents to participate in this study.

Genotyping of PLA2R and HLA-DQA1

The methods for selection of candidate SNPs of PLA2R and HLA-DQA1 and genotyping were described in the previous study[19]. SNPs of the candidate genes were obtained from previously published polymorphisms associated with PMN.

Genotype-phenotype correlation studies

Baseline clinical data were collected from all patients at diagnosis. PMN patients were divided into several subgroups based on the following parameters: 24 hours urinary protein excretion (24h-u-pro ≥ 3.5 g/d or < 3.5 g/d), renal function (eGFR ≤ 60 or > 60 mL/min/1.73 m²), and blood pressure ($\geq 140/90$ mmHg or

<140/90 mmHg). The eGFR calculation was using the CKD-EPI equation[32]. The association of alleles frequencies, genotype frequencies and different genetic models with clinical phenotype (24-h-pro, eGFR and blood pressure) in PMN patients was analyzed.

Detection PLA2R antibody in serum

120 PMN patients had anti-PLA2R antibodies detected to analyze the relationship between anti-PLA2R positivity and treatment response, as well as renal outcomes. The methods for measuring PLA2R antibody in serum were described in the previous study[19].

Definition

ESRD was defined as eGFR <15 mL/min/1.73 m², receiving dialysis therapy for more than 3 months or transplantation[33]. The primary outcome was renal progression, defined as a composite of ESRD, a reduction in eGFR by >30% from the baseline and doubling serum creatinine. Spontaneous remission (SR) included complete remission and partial remission. Complete remission (CR) was defined as 24 hours urinary protein excretion <500 mg per day with normal serum creatinine and serum albumin (≥35 g/L). Partial remission (PR) was defined as 24 hours urinary protein excretion of 0.5-2 g per day or <50% of baseline with normal serum creatinine and serum albumin level [24]. Patients who did not have complete or partial remission were called non- spontaneous remission. According our previous study, the PLA2R low-risk was defined as individuals with GG in rs2715918 and GG in rs4665143 within PLA2R. The rest were the PLA2R high-risk group. The HLA-DQA1 low-risk was defined as individuals with GG in rs2187668 within HLA-DQA1. The rest were the HLA-DQA1 high-risk group[19].

Statistical analysis

Continuous variables were presented as mean and standard deviation quartile spacing standard deviation (SD)Categorical variables were presented as median with interquartile ranges (IQR). Chi-square test was used to compare the classified variables between the two groups. Categorical variables were presented by proportions. Comparisons of continuous variables using t-test or one-way ANOVA. Hardy–Weinberg equilibrium (HWE) was determined by chi-square test. Logistic regression analysis was used to test three kinds of models of inheritance. Bonferroni adjustment was performed to correct P values (P_c). The association between gene mutation and kidney survival was analyzed by Kaplan–Meier.

Results

Baseline characteristics of PMN patients

The baseline characteristics of 314 (166 male and 148 female) PMN patients were described in Table 1. All those who participated in the study lived in Sichuan province for several generations and belonged to the Han ethnicity. The mean age at the time of renal biopsy was 49.1±13.5 years old, and the mean eGFR was 101.33±22.67 ml/min per 1.73 m². The median baseline proteinuria was 4.03 (range,2.34-6.20) g/24 h.

Genotype–phenotype correlations

Eight SNPs were successfully genotyped. The details of SNPs were shown in our pervious study[19]. All of them conformed to the Hardy-Weinberg equilibrium (HWE). We determined the association of alleles, genotype frequencies and different genetic models of candidate eight SNPs with phenotype (24h-u-pro, eGFR, blood pressure, respectively) in 314 PMN patients (Supplementary Table S1, Supplementary Table S2, Supplementary Table S3, respectively). The result revealed significant differences in alleles, genotype distributions, dominant, recessive, additive model of rs3828323 with hypertension ($P=0.008$, 0.029 , 0.037 , 0.034 , 0.012 , respectively). After Bonferroni adjustment, there was no statistical significance in the above variables ($P=0.064$, 0.232 , 0.296 , 0.272 , 0.096 , respectively). There was no association of alleles frequencies, genotype frequencies and different genetic models of rs3828323 with 24-h-pro or eGFR. No association was found between other SNPs and clinical phenotypes (24h-u-pro, eGFR, blood pressure). These results indicated the potential effects of rs3828323 on hypertension.

Follow-up data and treatment response

Among all the 314 individuals, 186 patients had complete follow-up data. Their baseline and follow-up characteristics were described in table 2. Forty-one (22.0%) patients reached the composite outcome during a median follow-up time of 18.6 (range, 6.7-45.5) months. The numbers of corticosteroid monotherapy, immunosuppression (Steroid + cyclophosphamide, Calcineurin inhibitor with or without steroid) and non-immunosuppression (with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers) were 29(15.6%), 112(60.2%), 45(24.2%), respectively. The result also showed that among 112 patients receiving immunosuppressive therapy, the numbers of complete remission, partial remission and non-spontaneous remission were 37(33.0%), 21(18.8%), 54(48.2%), respectively. Among 45 patients who did not receive immunosuppressive therapy, the numbers of complete remission, partial remission and non-spontaneous remission were 14(31.1%), 13(28.9%), 18(40.0%), respectively (Table 2).

Risk factors for no remission after treatment in PMN

According to the logistic regression analysis, we found urea (OR=1.184, 95%CI:1.030-1.361, $P=0.017$) was a risk factor for non-remission of the disease, eGFR (OR=0.984, 95%CI:0.970-0.998, $P=0.028$) and albumin (OR=0.922, 95%CI:0.880-0.966, $P=0.001$) were protective factors for non-remission of the disease (Table 3).

Genetic Variants and Immunosuppressive Therapy Response

Our previous studies showed interaction of rs2715918 GA/AA, rs4665143 GA/AA and rs2187668 GA/AA could significantly increase the risk for the development of PMN by 10.61-fold [19]. Therefore, in this study, we still choose these 3 SNPs and detected the association between genetic variants and response to immunosuppressive therapy. Genotypes under a dominant mode were considered the non-risk genotypes for PMN susceptibility and used as a reference. In univariate and multivariate logistic regression analysis, we found no statistical significance in response to immunosuppressive therapy between the reference and the genotypes carried risk alleles (Table 4).

Genetic variants and decline in renal function

Forty-one (22.0%) patients reached the composite outcome during a median follow-up time of 18.6 (range, 6.7-45.5) months. Kaplan–Meier analysis showed that for rs3828323, patients carrying CT/TT genotype achieved superior outcomes than CC genotype ($P=0.003$, Fig. 1). No associations were found with other SNPs.

Association between PLA2R/HLADQA1 Genotype and Anti-PLA2R Antibody

Our study included 314 PMN patients, of which 120 patients had anti-PLA2R antibodies in plasma tested. According to our previous study, we found that patients with low-risk SNPs had lower anti-PLA2R antibody positive rate than patients with high-risk SNPs[19]. Furthermore, we found there was no statistically significant difference in baseline characteristics between anti-PLA2R antibody positive group and anti-PLA2R antibody negative group (Table 5). Table 6 listed baseline characteristics in different combination groups. Both PLA2R and HLA-DQA1 high-risk group had the highest anti-PLA2R antibody positive rate (Table 6).

Discussion

In our retrospective study including 314 PMN patients, 8 SNPs of 2 genes (PLA2R and HLA-DQA1) were selected to analyze the association between SNPs and clinical phenotype in PMN patients. Rs3828323 T allele was marginally significantly associated with hypertension ($P=0.008$, $P_c=0.064$, $OR=1.821$). Among 186 patients who had complete follow-up data, forty-one (22.0%) patients reached the composite outcome during a median follow-up time of 18.6 (range, 6.7-45.5) months. The further study showed that patients carrying CT/TT genotype achieved better renal survival than patients carrying CC for rs3828323. The selected other candidate SNPs showed no association with clinical phenotype and renal outcomes in PMN patients.

Some of our results are consistent with the previous research. Liu et al found that rs35771982 and rs6757188 had no significant correlation with different clinical manifestations of PMN in a retrospective study and they were not independent risk factors for disease progression[14]. Kim et al identified that rs35771982 and rs3828323 were not associated with the prognosis of PMN patients[13]. However, in the current study, we found that patients with one or two T alleles (CT/TT) of rs3828323 had higher kidney survival than those without T allele (CC).

The natural course of PMN is diverse, with about one third of patients able to achieve spontaneous remission, about one third of patients with persistent proteinuria but long-term stable renal function, and another third of patients progressing slowly to end stage renal disease (ESRD)[10, 21, 22]. In our cohort, the median follow-up time of patients was 18.6 (range, 6.7-45.5) months. 55.4% ($n=103$) of them achieved spontaneous remission. In our data, urea ($OR=1.184$, 95%CI:1.030-1.361, $P=0.017$) was a risk factor, eGFR ($OR=0.984$, 95%CI:0.970-0.998, $P=0.028$) and albumin ($OR=0.922$, 95%CI:0.880-0.966, $P=0.001$) were

protective factors for non-remission of the disease. This finding is consistent with the previous literature where female was shown as a predictor of SR[10, 23].

Next, we compared genetic variants in terms of response to immunosuppressive therapy and renal outcomes. We found no statistically significant difference in response to immunosuppressive therapy. We also found that three risk genes for PMN development (A allele of rs2715918, A allele of rs4665143 and A allele of rs2187668) were not associated with renal outcomes and did not predict response to immunosuppressive therapy. However, we found that rs3828323 patients with one or two T alleles (CT/TT) had higher kidney survival than those without T allele (CC). In our previous study, rs3828323 was identified as a protective allele, indicating that a protective allele can not only reduce the susceptibility of PMN, but also serve as a predictor for renal outcomes. Liu et al found that two loci rs35771982 and 6757188 were associated with low remission rate after immunosuppressive therapy[14]. Bullich et al revealed that patients with both rs2187668 AA/AG and rs4664308 AA had better therapeutic effect with immunosuppressive agents, and slower progression of renal disease[17]. Our results are not consistent with the previous research. There are several potential explanations. PMN is a complex disease with both genetic and environmental factors contributing to the progress of the disease. Genetic heterogeneity among different races, or environmental factors, can influence disease progression. Furthermore, various clinical conditions of PMN patients may also have an impact on the disease progression. Further studies with a large sample size and longer duration of follow up is needed to explore the impact of SNP on treatment.

Nonsynonymous SNP rs3828323 C>T within PLA2R (Gly1106Ser) is located in a coding region of exon 24[16]. Previous literature and our study have confirmed that it is related to PMN susceptibility[16, 19, 24-26]. The SNP mutation sites of PLA2R can be found in both coding region or non-coding region, especially in intron or exon boundary region[16]. Any SNP may lead to different transcriptome lengths, which may lead to changes in protein function. A longer cut segment will form a stable transmembrane PLA2R protein, while a shorter cut segment will form a soluble enhanced PLA2R protein[27]. In conclusion, the SNP mutation of PLA2R gene may lead to the conformational change of PLA2R, and ultimately lead to the activation of PLA2R antibody, affecting the susceptibility and progress of the disease[24]. SNP mutation of HLA-DQA1 is more dangerous to PMN than PLA2R. There is a combined effect between these two mutations. Some researchers believed that HLA-DQA1 may be the dominant factor in the occurrence of PMN[12]. Its effect on the PMN autoantibody production may not only be through PLA2R pathway, but also through other ways[12]. In short, it seemed that the gene mutation of immunological immune system proteins (such as HLA-DQA1) is closely related to the gene mutation of glomerular component proteins (such as PLA2R), although the causal relationship between these two genes mutation is not yet clear. The direct relationship has not yet been established, but the whole mechanism is probably due to a complex system composed of trigger factors (immune system/HLA-DQA1), transduction pathway (PLA2R antibody) and target (glomerular antigen) related to[12]. Further researches on the occurrence and progress of SNP and PMN is needed.

Patients with the low-risk alleles of PLA2R and HLA-DQA1 had the lowest positive rate for anti-PLA2R antibody (41.6%). In contrast, patients with the high-risk alleles of PLA2R and HLA-DQA1 had the highest positive rate for anti-PLA2R antibody (87.8%). In all PMN patients who were tested for anti-PLA2R antibodies, treatment responses were seen in 71 patients. Among them, 57 patients had positive anti-PLA2R antibodies, of which 34 patients (59.6%) achieved spontaneous remission. Among 14 patients with negative anti-PLA2R antibodies, only 5 patients (35.7%) achieved spontaneous remission. Serum anti-PLA2R antibodies can be used in clinical diagnosis of PMN, especially in elderly patients with nephrotic syndrome or those who are not suitable for renal biopsy[28]. Anti-PLA2R antibody has high specificity and sensitivity. High titer of anti-PLA2R antibody indicates high risk of deterioration of renal function, low possibility of clinical remission, high recurrence rate and high risk of recurrence after renal transplant[8, 29, 30]. However, current literature reported the association between anti-PLA2R antibody and disease prognosis with inconsistent results[11, 24, 31]. suggesting that further higher quality research is needed in the future.

The major limitation of our study was the relatively short duration of follow up and small sample size. We were unable to fully explore the association between anti-PLA2R autoantibodies and renal disease progression due to the retrospective nature of this study.

Conclusion

In conclusion, to our knowledge, this is the first study identified that patients with CT/TT genotype achieved higher cumulative survival rate than patients with CC genotype for rs3828323. Our study also showed that rs3828323 T allele was marginally significantly associated with hypertension. Urea was a risk factor, and eGFR and albumin were protective factors for non-remission after treatment for PMN.

Abbreviations

CR: complete remission

ESRD: end stage renal disease

HLA-DQA1: human leukocyte antigen complex class II HLA-DQ α -chain 1

HWE: Hardy-Weinberg equilibrium

PLA2R: M-type phospholipase A2 receptor

PMN: primary membranous nephropathy

PR: partial remission

SNPs: single nucleotide polymorphisms

SR: spontaneous remission

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Sichuan Provincial People's Hospital. All patients gave fully informed written consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflict of interests.

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Authors' contributions

All authors have read and approved the manuscript for submission. Data collection (Shulei Fan, Qiuxia Wang, Wei Wang, Ping Zhang, Xiang Zhong), study design (Wei Wang, Guisen Li, Li Wang), statistical analyses (Shulei Fan, Shasha Chen, Wei Wang), writing (Shulei Fan, Wei Wang), language modification (Wang AY).

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Tables

Table 1 Baseline clinical characteristics of the study cohort

Characteristic	Patients with PMN (n=314)
Male/female	166/148
Age at biopsy (year)	49.1±13.5
Male (n, %)	166(52.9)
Scr (μmol/L)	68.60±26.80
Urea (mmol/L)	5.80±4.11
eGFR (ml/(min·1.73m ²))	101.33±22.67
Urine protein (g/24h)	4.03 (2.34,6.20)
HGB (g/L)	131.18±19.78
Alb(g/L)	27.20±15.84
SBP (mmHg)	128.06±15.83
DBP (mmHg)	78.23±11.24
Hypertension (n, %)	78(24.8)

Table 2 Baseline and follow-up clinical characteristics of the study cohort

Characteristic	Patients with PMN (n=186)
Baseline	
Age at biopsy (years)	49.1±13.4
Male (n, %)	102(54.8)
SCr (μmol/L)	68.9±22.5
eGFR (ml/min/1.73)	100.8±20.7
Urea (mmol/L)	5.6±2.2
Alb (g/L)	28.4±19.1 27.6(22.2, 31.4)
UA (μmol/L)	362.0±95.5
24h-u-pro (g/d)	4.17(2.31,7.34)
SBP (mmHg)	128.4±15.2
DBP (mmHg)	78.5±11.0
Hypertension (n, %)	47(25.3)
Follow-up	
SCr (μmol/L)	92.4±89.1
eGFR (ml/min/1.73)	90.6±29.9
Urea (mmol/L)	6.6±3.2
Alb (g/L)	36.4±8.5
UA (μmol/L)	373.3.0±106.6
24h-u-pro (g/d)	0.86(0.15,2.65)
Follow-up time (month)	18.6(6.7,45.5)
Endpoint event (n,%)	41(22.0)
Therapy	
Corticosteroid monotherapy(n,%)	29(15.6)
Immunosuppression(n,%)	112(60.2)
Non- Immunosuppression(n,%)	45(24.2)
Treatment effect	
Corticosteroid monotherapy	
CR/PR/non-SR(n,%)	12/6/11(41.4, 20.7, 37.9)

Immunosuppression	
CR/PR/non-SR(n,%)	37/21/54 (33.0, 18.8, 48.2)
Non- Immunosuppression	
CR/PR/non-SR(n,%)	14/13/18 (31.1, 28.9, 40.0)

The Endpoint event was defined as a combination of ESRD, a 30% reduction of eGFR from baseline and double times increasing of creatinine.

Table 3 Risk factors for no remission after treatment in PMN

Predictor	OR	95%CI	<i>P</i>
Gender (male)	0.760	(0.488-1.185)	0.226
Age	1.018	(0.995-1.040)	0.121
eGFR (ml/min/1.73 ^m)	0.984	(0.970-0.998)	0.028
Urea (mmol/L)	1.184	(1.030-1.361)	0.017
Alb (g/L ^m)	0.922	(0.880-0.966)	0.001
UA (μmol/L ^m)	0.987	(0.971-1.003)	0.655
24h-u-pro (g/d)	1.083	(0.998-1.174)	0.056
Blood pressure	0.9047	(0.474-1.727)	0.761
Anti-PLA2R-antibody positivity*	0.376	(0.112-1.266)	0.114
2715918 A allele carrier	1.045	(0.560-1.950)	0.891
4665143 A allele carrier	1.340	(0.651-2.759)	0.427
2187668 A allele carrier	0.945	(0.525-1.708)	0.851

*: Both follow-up data and the number of anti-PLA2R antibodies tested were 71.

Table 4 Logistic regression analyses between SNPs within HLA-DQA1 and PLA2R genes and primary membranous nephropathy response to immunosuppressive therapy

RS#		Remission	Non-Remission	Univariate Analysis ^a		Multivariate Analysis ^{a,b}	
		n(%)	n(%)	OR(95%CI)	<i>P</i>	OR(95%CI)	<i>P</i>
rs2715918	GG	39(67.3)	38(70.4)	1			
	GA	17(29.3)	13(24.0)	0.864(0.388-1.926)	0.721	1.273(0.545-2.978)	0.577
	AA	2(3.4)	3(5.6)				
rs4665143	GG	15(25.9)	9(16.7)	1			
	GA	20(34.5)	26(48.1)	1.744(0.691-4.403)	0.239	2.434(0.870-6.809)	0.090
	AA	23(39.6)	19(35.2)				
rs2187668	GG	34(58.6)	31(57.4)	1			
	GA	23(39.7)	22(40.7)	1.051(0.496-2.227)	0.897	1.139(0.521-2.494)	0.744
	AA	1(1.7)	1(1.9)				

^aUnivariate analysis considering a dominant model for HLA-DQA1 and a dominant model for PLA2R. The non-risk genotypes for primary membranous nephropathy susceptibility were considered as the reference.

^bAdjusted for proteinuria at diagnosis.

Table 5 clinical characteristics of PMN patients who detected circulating anti-PLA2R antibodies

Characteristic	anti-PLA2R(+)	anti-PLA2R(-)	<i>P</i>
Baseline	n=91	n=29	
Age at biopsy (years)	51.07±12.66	48.0±15.63	0.172
Male (n, %)	57(62.2)	15(51.7)	0.296
Cr (μmol/L)	73.17±25.05	75.60±52.47	0.736
eGFR (ml/min/1.73m ²)	95.77±21.78	100.84±27.78	0.311
Urea (mmol/L)	6.17±4.32	5.55±2.71	0.472
Alb (g/L)	27.97±26.29	27.7±7.64	0.959
24h-u-pro (g/d)	5.08±3.55	4.36±5.75	0.436
SBP (mmHg)	131.96±15.16	127.89±15.77	0.222
DBP (mmHg)	79.55±10.68	78.39±10.22	0.614

Table 6 Baseline characteristics of 120 PMN patients for detecting circulating anti-PLA2R antibody

	PLA2R low risk+ HLA low risk	PLA2R low risk+ HLA high risk	PLA2R high risk+ HLA low risk	PLA2R high risk+ HLA high risk	<i>P</i>
	n=12	n=7	n=60	n=41	
Male/female	8/4	4/3	36/24	24/17	0.963
Age(year)	48.33±15.47	54.86±15.08	49.95±15.28	52.71±9.30	0.564
Scr(μmol/L)	79.75±28.70	73.78±22.95	72.87±39.41	73.30±27.08	0.935
Urea(mmol/L)	5.78±1.90	6.08±2.74	6.43±5.19	5.48±2.21	0.707
eGFR(ml/(min·1.73m ²))	94.49±27.64	91.90±27.57	99.98±23.42	94.26±21.48	0.577
Urine protein (g/24h)	8.30±7.67	3.30±2.07	4.73±3.68	4.38±3.09	0.010
HGB (g/L)	132.25±17.11	132.14±15.66	132.08±15.72	133.07±17.52	0.993
Alb(g/L)	23.11±5.67	28.44±7.23	25.74±5.89	32.40±38.65	0.465
anti-PLA2R(+)/(-)	5/7	5/2	45/15	36/5	0.012
anti-PLA2R(+)(%)	41.6	71.4	75.0	87.8	

Figures

Figure 1

Survival analysis of time with outcome Kaplan–Meier analysis showed that with the prolongation of follow-up time, the CT/TT genotype for rs3828323 achieved higher cumulative survival rate ($P=0.003$) than CC genotype.

Supplementary Files

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- [SupplementaryTable.docx](#)