Research Square

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The Cutoff Value and Prognosis of Anti-PLA2R for Idiopathic Membranous Nephropathy: A Single-Center Retrospective Study From China

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Research Article

Keywords: the optimal cutoff value, anti-PLA2R, idiopathic membranous nephropathy, prognosis

Posted Date: February 1st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1237563/v1

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Abstract

Background Analyzing the antibody level of anti-phospholipase A2 receptor (anti-PLA2R) with idiopathic membrane nephropathy (IMN) and its correlation with clinical parameters and prognosis, and to explore optimal cut-off value for Chinese patients.

Methods All hospitalized patients with renal biopsy from April 2017 to November 2019 in Peking University Third Hospital whose clinical and pathological characteristics were analyzed, and the level of serum PLA2R antibodies was detected using the method of enzyme-linked immunosorbent assay (ELISA).

Result: The sensitivity, specificity, and Youden index of anti-PLA2R in the diagnosis of IMN in the Chinese patients were 85.7%, 88.3%, and 0.740 for the 2.5 RU/ml cut-off value; 77.8%, 96.0%, and 0.737 for the 6.3RU/ml cutoff value, respectively. The area under the ROC curve was 0.916. Compared with the high titer group, the low titer group had a higher serum albumin level (p=0.016), a lower cholesterol level (p=0.025) and a lower low density lipoprotein cholesterol (p=0.010). Multivariable Cox regression analysis showed that just immunosuppressive therapy (adjusted HR=4.656, 95 % CI 1.461-14.839, p=0.006) was associated with higher remission rate of IMN patients.

Conclusion: The best cutoff for ELISA method to detect anti-PLA2R antibodies in IMN patients is probably much lower (around 2-7 RU/ml) than that indicated by the manufacturer. The cut-off value of 6.3 RU/ml could get a higher sensitivity and not a lower specificity. If the IMN patients were treated actively, they maybe can get better prognosis.

Introduction

Idiopathic membranous nephropathy is a common cause of nephrotic syndrome in adult patients. One-third IMN patients will have persistent proteinuria and one-third IMN patients will progress to ESRD within 10 years. Therefore, it's very important to diagnosis the disease of IMN as soon as possible. The golden diagnosis standard of IMN was an invasive examination, that was renal pathology with potential risk of complications, such as bleeding, infection, and damage to other organs. And the patients with isolated kidney, coagulant function abnormality, uncontrolled hypertension and psychosis cannot be done renal biopsy. Thus, the early, accurate, non-invasive differentiation of IMN from other glomerular diseases is important.

Serum anti-PLA2R antibody which was first reported by Beck et al. in 2009[1, 2], can differential diagnosis of IMN from SMN or other nephropathies[2–6]. Anti-PLA2R tested by ELISA was used widely in clinic [7]. ELISA shows similar performance to IIF, with the advantages of quantitative results[8]. Anti-PLA2R values higher than 20 RU/mL that indicated by the manufacturer is positive to identify IMN from SMN and other nephropathies. Porcelli showed that the optimal cut-off value could be positioned at 14 RU/ml[9]. Chaofan Li from China found that the optimal cutoff value of anti-PLA2R was 7.45 RU/ml for distinguishing IMN

from non-IMN patients [10]. Other studies shows that the optimal cutoff value of anti-PLA2R were between 2.0 and 2.7 RU/ml to diagnosis IMN from other diseases[1, 7, 11–13].

Accordingly, in the literature, the diagnostic accuracy of PLA2R antibodies in IMN patients is variable. Therefore, we aimed to summary our data to check the optimal cutoff value of anti-PLA2R by commercial ELISA in order to get more experience in the diagnosis value of anti-PLA2R on IMN patients and analyze the correlation between anti-PLA2R levels and clinical parameters, such as serum creatinine, serum albumin, 24-hour urinary protein and estimated glomerular filtration rate, also and prognosis. Maybe some IMN patients don't need to do the renal biopsy.

Methods

This study carried out in accordance with the Helsinki Declaration and the study protocol was approved by the Ethics Review Committee of Third Peking University Hospital in China (IRB00006761-M2021534). Patient consent for inclusion was waived by the Ethics Review Committee of Third Peking University Hospital in China.

Study population

773 hospitalized patients were enrolled from April 2017 to November 2019 in Peking University Third Hospital. There were 252 IMN patients and 521 non-IMN patients. The inclusion criteria were as follows: 1) more than 18 years old, 2) having anti-PLA2R results before renal biopsy, 3) having results of renal biopsy. The exclusion criteria were as follows: 1) having received immunosuppressive therapy before kidney biopsy, 2) the results of the clinical results cannot be founded. The diagnosis of IMN was made by the kidney biopsy which featured capillary wall thickening, granular IgG and C3 along capillary walls on immunofluorescence, and subepithelial deposits on electron microscopy.

The clinical data of all patients were collected and analyzed retrospectively. 521 non-IMN disease was contained IgA nephropathy(n=238) , minimal change disease(MCD) (n=55), focal proliferative glomerulosclerosis(FSGS) (n=12), diabetic nephropathy(DN) (n=56), lupus nephritis(LN)(n=25, including 9 MN patients), hepatic B virus glomerulonephritis(HBV-GN) (n=5, including 4 MN patients), hypertensive renal damage(n=10), interstitial nephritis (n=30), ANCA-associated glomerulonephritis(n=6), primary renal amyloidosis(n=7), 14 purpura nephritis(n=14), membranoproliferative glomerulonephritis(n=5), thrombotic microangiopathy(n=6), thin basement disease(n=8), acute tubular necrosis(n=8) and mild glomerular ischemia with chronic interstitial fibrosis(n=13) and other few nephropathies(n=10).

General clinical parameters

The clinical data of all patients were from the baseline results before immunosuppressive therapy. General information included age, sex, edema, and hypertension. Laboratory parameters included urinary red blood cell (U-RBC), 24-hour urinary protein, serum albumin, serum creatinine, estimated glomerular filtration rate (eGFR), cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein

cholesterol, anti-PLA2R antibodies and renal biopsy results. Values of eGFR were calculated by the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.

Anti-PLA2R detection

Serum anti-PLA2R titer was assessed by an ELISA method (kit purchased from Euroimmune, Lubeck, Germany). The EUROIMMUN manufacturer suggested reporting results lower than 14 RU/mL as negative, those between 14 and 20 RU/mL as borderline and those higher than 20RU/ml as positive. In this study, anti-PLA2R value lower than 20 RU/mL was defined as negative. According to the anti-PLA2R data in the IMN group, low titer group was considered anti-PLA2R value at lower than 20 RU/mL, middle titer group between 20 and 150 RU/mL, and high titer group at equal and more than 150RU/ml.

Statistical analysis

All continuous dates were expressed as mean±standard deviation, and categorical dates were expressed as numbers (percentage). Student t-tests and ANOVA were used appropriately to determine differences between groups. Chi-square tests was performed for the comparison of categorical data. Spearman test was performed for the correlations between anti-PLA2R and other parameters. Kaplan-Meier and multivariate Cox's proportional hazard model, in which all the significant variables ($p<0.15$) from the univariate analysis were included, was using to analyze the non-remission risks. Variables in the final multivariate Cox model were selected in a enter manner. Receiver operating characteristic (ROC) curve was used to analyze the optimal cutoff value. P values less than 0.05 were considered to be statistically significant. Data management and analysis were performed using SPSS software, version 22.0.0.0 (IBM SPSS Statistics 22).

Results

General baseline parameters

The average age and anti-PLA2R antibody in the IMN group were higher than that in the non-IMN group (49.39±0.94 vs. 41.88±0.66years, p=0.000; 153.09±22.43 vs. 1.99±0.23RU/ml, p=0.000). In the non-IMN group, 98.8% patients' anti-PLA2R levels were lower than 20RU/ml (Fig. 1). There was no statistically difference in the male sex ratio between the IMN group and non-IMN group (58.7% vs. 56.2%, p=0.512).

The overall positive rate of anti-PLA2R in the non-IMN group was 1.2% (Fig. 1). There were six non-IMN patients with anti-PLA2R value more than 20 RU/mL, one of them was SMN with lupus nephritis (table1). There were 9 patients with secondary MN in all 25 patients with lupus nephritis. The second positive anti-PLA2R non-IMN patient was induced by the drug of dabigatran. The third patient was a DN patient with typical renal biopsy and twenty years' diabetes mellitus history. The fourth and fifth MCD patients were complete remission in two months with mono-glucocorticoid drug. The sixth patient was a typical IgA nephropathy. In SMN, the median level of anti-PLA2R was less than 2 RU/mL, and the positive rate of anti-PLA2R was only 7.1%.

The optimal cutoff value of anti-PLA2R

We performed a ROC curve analysis to find the optimal anti-PLA2R cut-off value in Chinese IMN patients (Fig. 2). ROC curve analysis showed that 2.5RU/ml was the optimal cutoff value with the highest Youden index (0.740). At the regular anti-PLA2R cut-off value of 20 RU/ml, the specificity was 98.8%, but the sensitivity was only 67.5% in our study. Table 2 show the diagnostic efficiency at different anti-PLA2R cutoff values. The area under the ROC curve was 0.916 (95% CI 0.890–0.942, p=0.000).

Correlations between anti-PLA2R and parameters

There was a statistically positive correlation between anti-PLA2R and 24-hour urinary protein in the IMN patients (r=0.341, p=0.000) (Fig. 3). In contrast, there was a significant negative correlation between anti-PLA2R and albumin (r=−0.274, p=0.000), and no significant correlation between anti-PLA2R and eGFR (r=-0.059, p=0.356) in the IMN patients (Fig. 3).

Comparisons of baseline characteristics among subgroups in the IMN group

In this clinical study, 252 patients with IMN were divided into three subgroups according the anti-PLA2R values: low titer group (<20 RU/ml, n=84), middle titer group (20-150 RU/ml, n=95), and high titer group (>150 RU/ml, n=73). Comparisons of clinical features among the three subgroups were listed in Table 3. The results showed that according to the higher and higher serum anti-PLA2R levels, 24-hour urinary protein also became higher and higher (p=0.000). Compared with the high titer group, the low titer group had a higher serum albumin level (p=0.016), a lower cholesterol level (p=0.025) and a lower low density lipoprotein cholesterol (p=0.010). However, differences in other indexes, such as age, sex, hypertension rate, serum creatinine, eGFR, urinary red blood cell, and prognosis had no statistical significance.

Follow up of the IMN patients

Among 252 IMN patients, 136 patients were treated in our hospital, 122 patients were analyzed their prognosis except for 14 patients without their anti-PLA2R value at the last follow up. The remission rates were becoming higher and higher when the immunosuppressive therapy using rates were more and more from the low titer group, middle titer group to the high titer group. But the remission rate and immunosuppressive therapy using rate had no significance different among the three groups. Although the anti-PLA2R values in the high titer group were higher than those in the low titer group, 24-hour urinary protein in the high titer group were lower than those in the low titer group (Table4). Non-remission IMN patients were only 21 patients, however there were 115 patients who got complete remission or partial remission. Multivariable Cox regression analysis showed that immunosuppressive therapy (adjusted HR=4.656, 95 % CI 1.461-14.839, p=0.006) was associated with higher remission rate of IMN patients. (Table 5)

Discussion

The positive rate and level of anti-PLA2R in our study were significantly higher in IMN patients than in non-IMN patients, which indicated that it was a specific biomarker in the differential diagnosis of IMN. Analyzing the baseline characteristics of the participants enrolled in our study, no significant differences were observed in the Scr, U-RBC, hypertension rate and eGFR measurements among the three groups. The high titer IMN group had a higher urinary protein, and a lower albumin than those in the low and middle titer groups. It was similar to the study by Kim et al. which found that albumin was lower in the high titer group and that no significant difference existed in serum creatinine[14]. In both Chinese studies, the high titer group also had higher levels of 24-hour urinary protein, but there was no difference in albumin [15, 16]. And Li et al. found that the positive group had a higher baseline urine protein level, a lower albumin level, but a lower eGFR than the negative group [16]. For these differences, the effect of ethnic background cannot be ignored. Different stages and statuses of disease when subjects were enrolled also account for the discrepancies.

Anti–phospholipase A2 receptor was a biomarker for diagnosis, activity evaluation, therapy monitoring, and prognostic estimation of IMN. The optimal cutoff value of anti-PLA2Rvalue by ELISA was variable in different studies from different countries. The EUROIMMUN manufacturer suggests reporting anti-PLA2R values higher than 20RU/ml as positive. In our study, using cut-off of 20 RU/ml the specificity can be high to 98.8%, but the sensitivity was just 67.5%. Behnert[17] reported a sensitivity of 82.2%, with a specificity of 89.7% respectively using cut-off value of 20 RU/ml in American and German cohorts of patients. In a Chinese cohort, Dou et al.[11] reported that at different cut-off value of 20 RU/ml, specificity was 97.3%, while sensitivity was 60.2%. But there were also studies from China[1, 14] and Japan[18] when using the cutoff value of 20 RU/ml the sensitivity was just between 44.1% and 50.9%, what's more the sensitivity in a study from Australia was just 25%.

Anti-PLA2R values higher than 14RU/ml were considered as borderline to diagnosis IMN. Behnert et al. [17] reported a sensitivity of 86.1%, with a specificity of 84.5% using cut-offs of 14 in American and German cohorts of patients. Dou et al. [11] reported that at cut-off value of 14RU/ml, specificity was 97.3%, while sensitivity was 65.3%, suggesting that 14 RU/ml should be applied to obtain higher sensitivity with no change in the specificity values in China.

In order to get a higher diagnosis sensitivity, researchers have been exploring whether a lower cutoff value can be available. We found that 2.5RU/mL was the optimal cutoff with the highest Youden index (0.740), the sensitivity was 85.7%, the specificity was 88.3%, the area under the ROC curve was 0.916 (95% CI 0.890–0.942, p=0.000). In the study by Timmermans et al.[7] that sensitivity could be improved to 72% without affecting the specificity by reducing the cut-off value to 2 RU/ml. Furthermore, Liu et al. [1] found that the optimal cut-off value was 2.6 RU/ml with a sensitivity of 78.9% and a specificity of 91.7% in 57 Chinese IMN patients and two studies indicated that the optimal cut-off value was 2.7 RU/ml with a sensitivity 83.3%-88.1% and a specificity 95.1%-96%[16, 19].

The optimal cutoff value of 7.45 RU/mL was preferred in a China study which sensitivity was 83.3% and specificity was 95.1%[10]. In our study, when the cutoff value was 6.3, the sensitivity was 77.8%, the specificity was 96.0%, and the Youden index was 0.737. Take altogether, 2.5 RU/ml and 6.3 RU/ml were both optimal cutoff values, 2.5 RU/ml can get higher sensitivity and 6.3 can get higher specificity. In our mind, we thought that maybe 6.3 RU/ml seemed to be much better to be the optimal cutoff value which can get a higher specificity and a not much lower sensitivity. The cut-off value of 6.3 RU/ml was recommended for the use of anti-PLA2R for the diagnosis of IMN in Chinese patients based on the ELISA.

Can we use double criterions for blood PLA2R? Anti-PLA2R>20RU/ml is used as the specific index to diagnose PLA2R related IMN without renal biopsy pathology, and the error probability is less than 2%; Anti-PlA2R<2RU/ml is used as the sensitivity index to deny PLA2R related IMN. If the clinical characteristics of patients with anti-PLA2R 2-20RU/ml are consistent with IMN, it may still be PLA2R related IMN. Whether renal biopsy is needed should be depend on the patient's clinical characteristics.

In our study, the remission rate and immunosuppressive therapy in the high titer group were higher than those in the low and middle titer groups, but there was no significant difference. Multivariable Cox regression analysis showed that immunosuppressive therapy was the only factor that associated with higher remission rate of IMN patients. In other words, if the severe IMN patients receive treatment in time, they also can get a high remission rate [20].So we should pay more attention at the immunosuppressive therapy in order to get better prognosis. However, it was quite different from these studies. For example, a reduction in the anti-PLA2R value correlated with better prognosis in IMN patients [6, 21-23], while persistence of anti-PLA2R value was associated with clinical resistance[22, 23]. Lower anti-PLA2R value at baseline and after 6 months were associated with IMN remission[19]. What caused these different results in different studies?

First, in our study anti-PLA2R was correlated with 24-hour urinary protein, albumin, eGFR, TC and LDL. However, correlations between anti-PLA2R and albumin was negative, and others were positive. Furthermore, there were significant differences in 24-hour urinary protein, albumin, and eGFR, TC and LDL among the low titer subgroup and high titer subgroup. Other studies were different with our results. For example, Li et al found that 24-hour urinary protein positively correlated with anti-PLA2R, while albumin, and serum creatinine did not correlate[5]. Another study showed that serum anti-PLA2R antibody levels were correlated with serum albumin, serum creatinine, eGFR, and proteinuria [24]. Two Japanese studies indicated that anti-PLA2R negatively correlated with albumin, but its correlations with serum creatinine and 24-hour urinary protein were also different in these two studies[18, 25]. Li YQ revealed that the correlations of anti-PLA2R antibody value with urine protein and cholesterol were positive, but the correlations of anti-PLA2R antibody value with albumin and eGFR were negative[16]. Secondly, the IMN patients were from different races in different countries; Third, small sample size and patient selection bias may also be important reasons for the difference in results.

This study suffers from several limitations. Firstly, it is a single-center retrospective study. Secondly, because patients receiving immunosuppressive therapy were excluded, anti-PLAR level of them at onset could not be analyzed and selection bias could not be neglected in this retrospective study. Third, the findings may reflect practice patterns in an East Asian population. A large-sample multi-center prospective study is needed to further validate these findings.

In conclusion, this study showed that the best cutoff value of anti-PLA2R antibodies for the widely used ELISA method to detect anti-PLA2R antibodies in IMN patients is probably much lower (around 2-7RU/ml) than that indicated by the manufacturer, thereby relevantly increasing assay sensitivity, the best cut-off value could be positioned at 6.3 RU/ml in our study. If the IMN patients were treated actively, they maybe can get better prognosis.

Declarations

Ethics approval and consent to participate

This study carried out in accordance with the Helsinki Declaration and the study protocol was approved by the Ethics Review Committee of Peking University Third Hospital in China (IRB00006761-M2021534). Ethical approvals were granted by the Ethics Review Committee of Peking University Third Hospital. Patient consent for inclusion was waived by the Ethics Review Committee of Third Peking University Hospital in China

Consent for publication

Not Applicable.

Availability of data and materials

The raw datasets analyzed in this study are available from the corresponding author upon reasonable request and with permission of the Institutional Review Board.

Competing interests

There are no conflicts of interest to declare.

Funding

Danxia ZHENG is supported by the idiopathic membranous nephropathy cohort study for Clinician Scientists, Peking University Third Hospital (BYSYDL2021017).

Authors' contributions

Data were collected and analyzed by Hongxia Guo, Yao Yao, Jiansuo Zhou, and Danxia Zheng with suggestions from other authors. The manuscript was written by Hongxia Guo, edited by Danxia Zheng

and Yue Wang, and approved by all authors.

Acknowledgements

We are very grateful to all the patients for their selfless dedication in this study and want to express our deepest sympathy to all our patients and their relatives. We also want to express our thanks to our fellow doctors and nurses who are providing clinical diagnosis and treatment to the nephrology patients.

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Tables

Table1. Characteristics of the positive anti-PLA2R non-IMN patients

Characteristic	Age/sex	Serum albumin	Urine protein	Anti-PLA2R	Renal biopsy
1	63/F	2.42	39.3	33.57	focal proliferative glomerulitis
2	50/F	32.3	1.736	59.46	lupus nephritis
3	52/M	22.6	8.9	50.53	Minimal change disease
4	66/M	32	11.1	46.84	Minimal change disease
5	44/F	33.7	6.6	52.87	IgA nephropathy
6	59/M	32.7	1.4	31.41	diabetic nephropathy

positive anti-PLA2R: anti-phospholipase A2 receptor antibody value more than 20RU/ml.

Table 2. The efficiency of anti-PLA2R for diagnosing IMN at different cutoff values

Cutoff, RU/mL	Sensitivity, %	Specificity, %	Youden index
2	86.9	83.7	0.706
2.5	85.7	88.3	0.740
6.3	77.8	96.0	0.737
14	70.6	98.5	0.691
20	67.5	98.8	0.663

Anti-PLA2R, anti-phospholipase A2 receptor antibody.

Table3 Baseline characteristics of anti-PLA2R-positive IMN patients and anti-PLA2R-negative IMN patients

Characteristic	Low titer (n=84)	Middle titer (n=95)	high titer (n=73)	F	P
Male, n (%)	52(61.9)	59(62.1)	38(52.1)		0.345
Age, yr	47.4±1.7	48.4±1.5	52.6±1.6	2.676	0.071
Hypertension, n (%)	36(43.4)	53(55.8)	41(56.2)		0.172
Anti-PLA2R, RU/mL	5.3±0.6*&	72.4±3.8&#	425.5±67.4*#	40.880	0.000
Urinary protein, g/24 h	4.9±0.4*&	6.6±0.4&#	8.6±0.7*#	-4.757	0.000
U-RBC, n (%)	52(61.9)	43(46.2)	44(60.3)		0.071
Albumin, g/L	32.0±0.7*&	29.6±0.6&	28.2±0.7*	7.690	0.001
Scr, mg/dL	75.5±3.0	71.4±2.3	77.4±5.4	0.790	0.455
eGFR, ml/min/1.73 m^2	98.0±3.0	102.0±2.2	93.9±2.6	2.631	0.074
Cholesterol, mmol/L	6.1±0.2*&	7. 7±0.3&	8.4±0.3*	15.417	0.000
LDL, mmol/L	4.0±0.2*&	4.8±0.2&	5.4±0.3*	8.648	0.000

PLA2R phospholipase A2 receptor; U-RBC urinary red blood cell; Scr serum creatinine; eGFR estimated glomerular filtration rate; LDL low density lipoprotein cholesterol; RAS renin–angiotensin system; CTX Cyclophosphamide; CsA Cyclosporine; RTX Rituximab; *: $p < 0.05$ for the negative versus positive group; $p < 0.05$ for the high titer versus low titer group.

low titer group was considered anti-PLA2R value at lower than 20 RU/mL, middle titer group between 20 and 150 RU/mL, and high titer group at equal and more than 150RU/ml.

Table4 Baseline characteristics of IMN patients with prognosis before renal biopsy and at last follow up

Characteristic	Low titer (n=40)	Middle titer (n=44)	high titer (n=38)	F	P
Male, n (%)	23(57.5)	29(65.9)	18(47.4)		0.239
Age, yr	49.85±2.54	47.34±2.16	50.18±2.17	0.473	0.624
Hypertension, n (%)	17(42.5)	24(54.5)	22(57.9)		0.353
Baseline					
Anti-PLA2R, RU/mL	6.2±0.9*&	78.4±5.4&#	338.5±33.4*#	89.423	0.000
Urinary protein, g/24 h	5.5±0.6*	6.8±0.5	7.7±0. 7*	3.292	0.041
U-RBC, n (%)	26(65.0)	18(42.9)	24(63.2)		0.080
Albumin, g/L	30.0±1.0	29.9±0.9	27.8±1.0	1.651	0.196
Scr, mg/dL	75.1±3.9	71.8±2.6	74.4±3.7	0.259	0.772
eGFR, ml/min/1.73 m2	96.8±3.6	103.6±2.9	94.9±3.4	1.882	0.156
Cholesterol, mmol/L	6.6±0.4*#	7.2±0.3	9.0±0.5*#	9.200	0.000
LDL, mmol/L	4.3±0.3*	4.6±0.3	5.9±0.4*	5.966	0.003
Last follow up					
Albumin, g/L	38.4±1.1	38.9±0.9	38.0±0.8	0.214	0.808
Urinary protein, g/24 h	1.9±0.7*	1.8±0.6	1.5±0.4*	0.162	0.850
Anti-PLA2R, RU/mL	2.0±0.3*	8.6±2.4#	26.7±9.9*#	5.143	0.007
Remission	30(75.0)	37(84.1)	36(92.3)		0.250
RAS blockers	35(87.5)	37(84.1)	28(73.7)		0.256
immunosuppressive therapy (%)	21(52.5	27(61.4)	27(71.1)		0.243

PLA2R phospholipase A2 receptor; U-RBC urinary red blood cell; Scr serum creatinine; eGFR estimated glomerular filtration rate; LDL low density lipoprotein cholesterol; RAS renin–angiotensin system; CTX Cyclophosphamide; CsA Cyclosporine; RTX Rituximab; *: $p < 0.05$ for the negative versus positive group; $p < 0.05$ for the high titer versus low titer group.

low titer group was considered anti-PLA2R value at lower than 20 RU/mL, middle titer group between 20 and 150 RU/mL, and high titer group at equal and more than 150RU/ml.

Table5 Multivariable Cox regression analysis results of IMN patients with prognosis

Parameters	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Gender, male	0.760 (0.299–1.934)	0.565	-	-
Age, years	0.996(0.965–1.028)	0.785	-	-
Hypertension	1.405(0.550–3.591)	0.478	-	-
anti-PLA2R Ab, U/mL	0.996(0.991–1.001)	0.106	1.003(0.999-1.008)	0.174
Proteinuria, g/24 h	0.980(0.863–1.112)	0.752	-	-
U-RBC	1.337(0.526–3.400)	0.542	-	-
Albumin, g/L	0.990(0.920–1.065)	0.790	-	
eGFR, mL/min/1.73 m2	0.999(0.978-1.020)	0.913	-	
Cholesterol, mmol/L	0.868(0.713-1.057)	0.160	-	
LDL, mmol/L	0.837(0.654-1.071)	0.156	-	
RAS blockers use (%)	0.632(0.172–2.324)	0.490	-	
Mono-glucocorticoid	0.970(0.256–3.672)	0.964	-	
Immunosuppressive therapy (%)	4.972(1.575–15.690)	0.006	4.656(1.461-14.839)	0.009

PLA2R phospholipase A2 receptor; U-RBC urinary red blood cell; Scr serum creatinine; eGFR estimated glomerular filtration rate; LDL low density lipoprotein cholesterol; RAS renin–angiotensin system; CTX Cyclophosphamide; CsA Cyclosporine; RTX Rituximab; *: $p < 0.05$ for the negative versus positive group; $p < 0.05$ for the high titer versus low titer group.

low titer group was considered anti-PLA2R value at lower than 20 RU/mL, middle titer group between 20 and 150 RU/mL, and high titer group at equal and more than 150RU/ml.

Figures

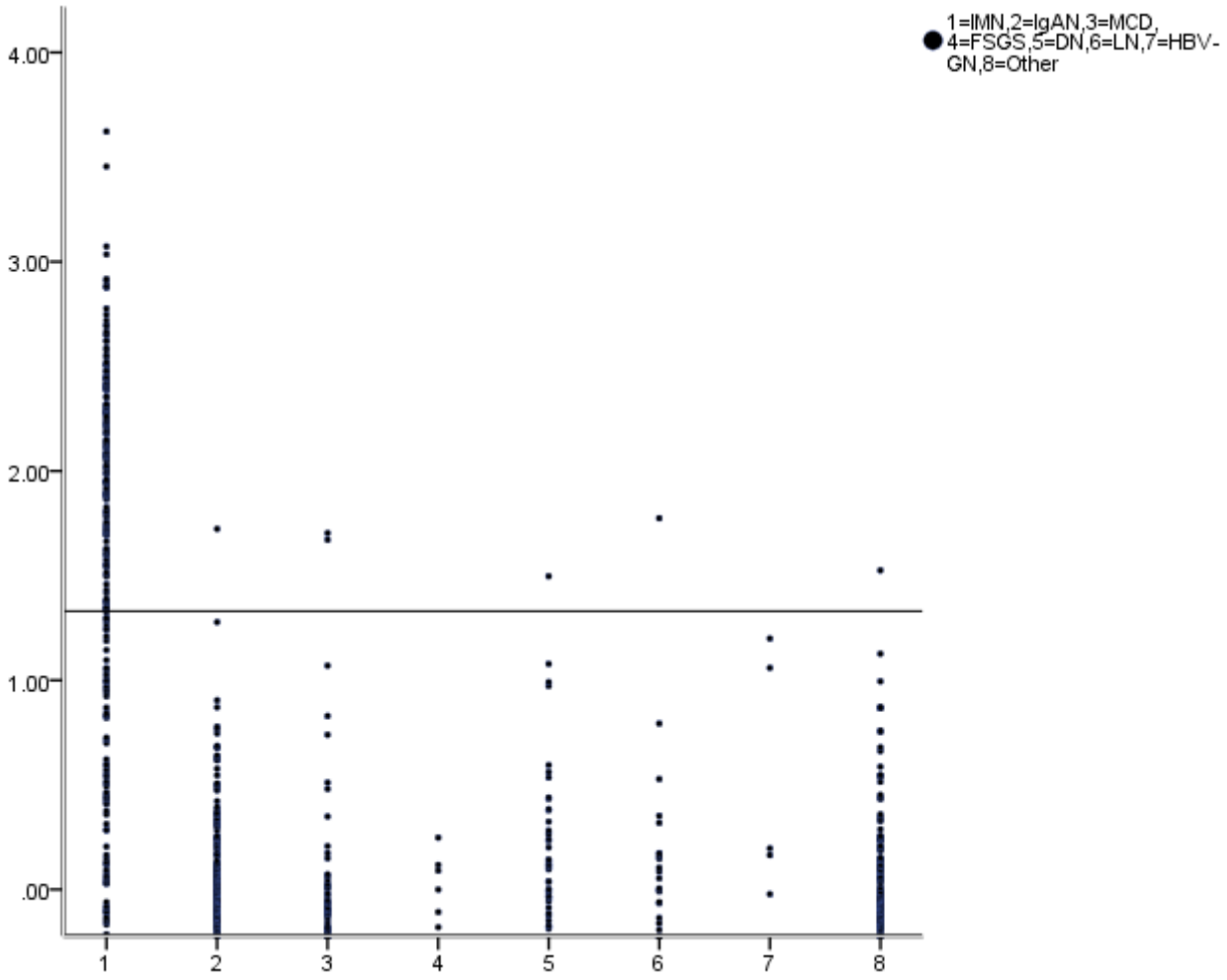

Figure 1

Distribution of anti-PLA2R autoantibody levels in IMN patients and non-IMN patients

IMN: idiopathic membranous nephropathy; IgAN: IgA nephropathy; MCD: minimal change disease; FSGS: focal proliferative glomerulosclerosis; DN: diabetic nephropathy; LN: lupus nephritis; HBV-GN: hepatic B virus glomerulonephritis.

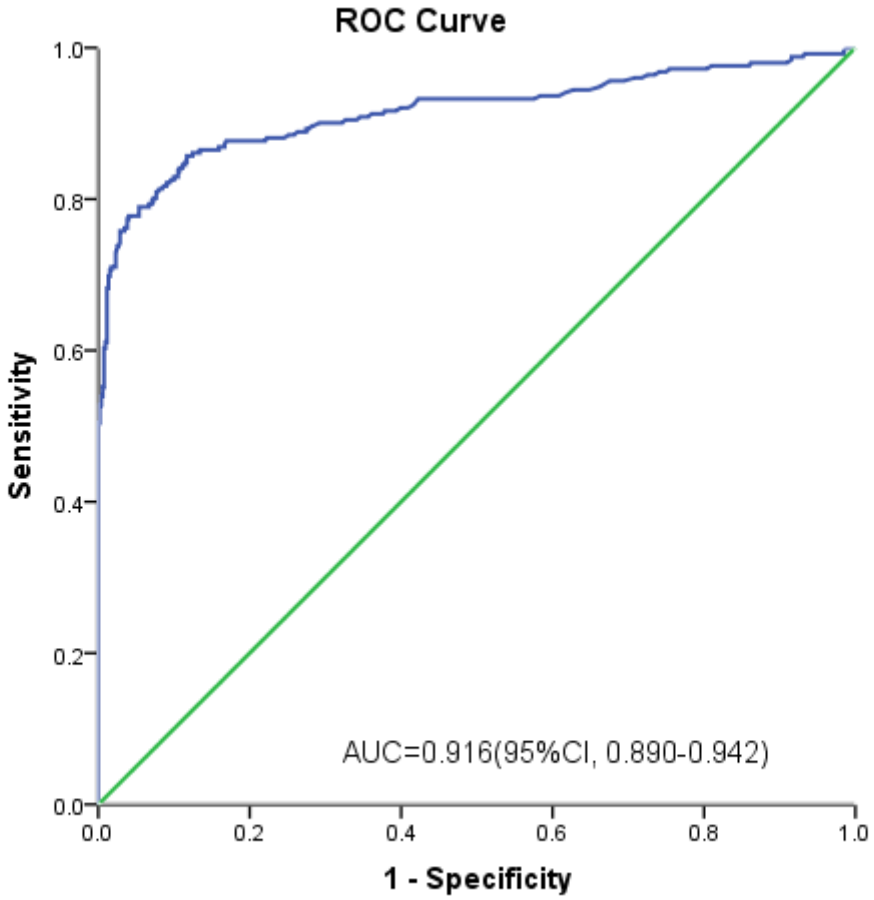

Figure 2

ROC curve of anti-PLA2R for the identification of patients with IMN

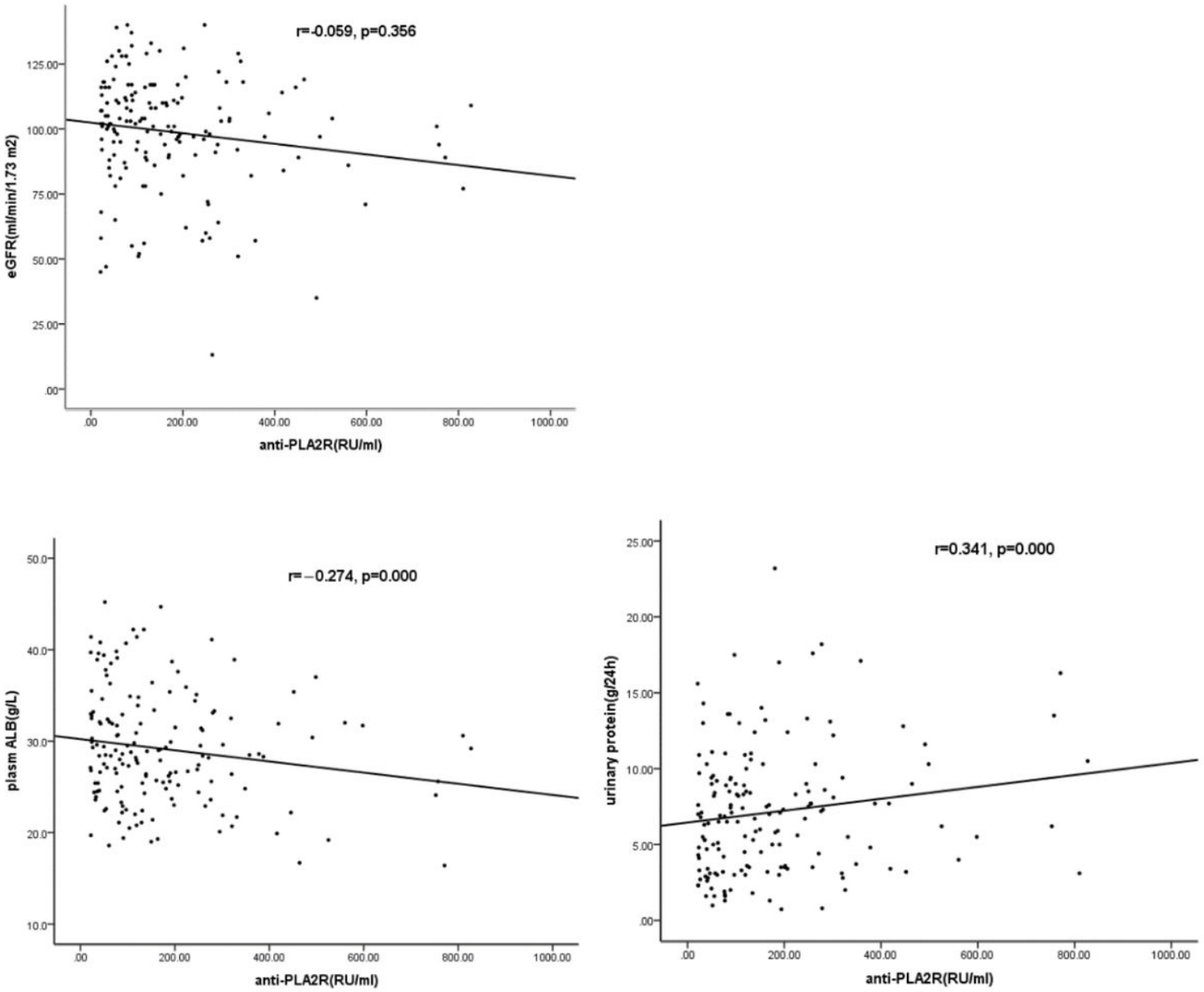

Figure 3

Correlations between anti-PLA2R and other clinical parameters in IMN patients(n=252, Spearman test)