

## Original Article

# Comparison of the efficacy and impact on coagulation function of different rituximab dosage regimens in the treatment of membranous nephropathy

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Received November 3, 2024; Accepted January 5, 2025; Epub March 15, 2025; Published March 30, 2025

**Abstract:** Objective: To compare the efficacy and safety of two rituximab (RTX) dosage regimens - 1 g and 375 mg/m<sup>2</sup> - in patients with idiopathic membranous nephropathy (IMN), focusing on their effects on coagulation function. Methods: We conducted a single-center, retrospective cohort study involving 323 IMN patients treated at Baoji High-Tech Hospital between May 1, 2022, and February 28, 2024. Patients were categorized into a standard-dose group (375 mg/m<sup>2</sup>, n=157) and a low-dose group (1 g, n=166) based on their RTX regimen. We compared clinical remission rates, relapse rates, adverse reactions, and changes in coagulation parameters (thrombin time [TT], prothrombin time [PT], fibrinogen [Fib]) between the groups. Results: Baseline characteristics, including age, gender, BMI, comorbidities, and immune indices, were similar between the groups (all P>0.05). Complete remission rates were 28.7% in the standard-dose group and 31.3% in the low-dose group, with overall response rates of 82.2% and 71.7%, respectively. Relapse rates were 19.1% and 19.3%, showing no significant differences (P>0.05). No significant differences in renal function, serum protein, urine protein, or PLA2R levels were observed between the groups (all P>0.05). Coagulation parameters remained unchanged before and after treatment (all P>0.05). Adverse reactions, including infections, infusion reactions, liver dysfunction, and gastrointestinal symptoms, occurred at similar rates in both groups (all P>0.05). Multivariate analysis identified BMI (OR=1.710, P<0.001), history of diabetes (OR=7.186, P=0.002), 24-hour urine protein at 6 months (OR=2.227, P<0.001), and PLA2R levels (OR=1.391, P<0.001) as independent risk factors for hypercoagulability. Conclusion: Both 1 g and 375 mg/m<sup>2</sup> RTX regimens exhibit comparable efficacy and safety in IMN patients, without significantly affecting coagulation function. Treatment should be individualized based on factors such as BMI, diabetes history, urine protein levels, and PLA2R levels to optimize coagulation risk management.

**Keywords:** Idiopathic membranous nephropathy, rituximab, dosage comparison, efficacy, safety, coagulation function

## Introduction

Membranous nephropathy (MN) is one of the leading causes of nephrotic syndrome (NS) in adults in China, excluding diabetic nephropathy, and its global incidence is rising, particularly among middle-aged and elderly males [1]. MN is classified into idiopathic membranous nephropathy (IMN) and secondary membranous nephropathy (SMN), with approximately 80% of cases being idiopathic and the remaining 20% secondary to conditions such as systemic lupus erythematosus (SLE), viral infections, malignancies, or certain medications [2,

3]. The hallmark pathological feature of MN is the subepithelial deposition of immune complexes on the glomerular basement membrane, leading to thickening and damage of the glomerular filtration barrier. Clinically, this manifests as massive proteinuria, hypoalbuminemia, and edema [4]. Without timely intervention, MN can progress to chronic kidney disease or end-stage renal disease, significantly affecting patient prognosis.

Recent advances in the understanding of MN pathogenesis have highlighted the critical role of B cells. The identification of M-type phospho-

lipase A2 receptor (PLA2R) [5] and thrombospondin type-1 domain-containing 7A (THSD7A) [6, 7] has facilitated both diagnosis and treatment. Traditional immunosuppressive therapies, such as glucocorticoids combined with alkylating agents or calcineurin inhibitors (CNIs), are effective in reducing proteinuria but are often associated with high relapse rates and significant adverse effects, including bone marrow suppression, infections, and nephrotoxicity [8, 9]. These limitations underscore the need for safer and more effective treatment alternatives.

Rituximab (RTX), a human-mouse chimeric monoclonal antibody targeting the CD20 antigen on B cells, selectively depletes B lymphocytes and inhibits B cell-mediated immune responses [10]. Initially approved for treating non-Hodgkin lymphoma (NHL) [11] and chronic lymphocytic leukemia (CLL) [12], RTX has since been increasingly used in autoimmune diseases, including rheumatoid arthritis (RA) [13]. In recent years, RTX has demonstrated significant efficacy in treating IMN, leading to its recommendation as a first-line treatment for medium- and high-risk MN patients in the 2021 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines [14].

Although RTX's efficacy in treating IMN is well established, the optimal dosage regimen remains debated. The 2020 "Consensus on Rapid Infusion of RTX in China" [15] recommends the 375 mg/m<sup>2</sup> dose, originally used for non-Hodgkin lymphoma. However, the 2022 "Expert Consensus on the Use of RTX in Membranous Nephropathy" [16] suggests that both the 1 g and 375 mg/m<sup>2</sup> regimens can be used for IMN treatment. The existence of these two regimens highlights the need for individualized therapy, but direct comparative studies are scarce [17].

Coagulation dysfunction is another critical concern in MN patients, particularly those with nephrotic syndrome, who are at increased risk of thromboembolic events [18]. Hypoalbuminemia and hyperlipidemia, common in nephrotic syndrome, contribute to a hypercoagulable state, elevating the risk of complications such as deep vein thrombosis and pulmonary embolism [19].

This study aims to compare the efficacy and safety of the 1 g and 375 mg/m<sup>2</sup> RTX dosage

regimens in IMN patients and evaluate their effects on coagulation function. By providing evidence for the optimal dosing strategy, we aim to contribute to personalized treatment plans for IMN and offer guidance for monitoring and managing coagulation function in these patients.

### Materials and methods

#### *Study design*

This single-center, retrospective cohort study included 323 patients diagnosed with idiopathic membranous nephropathy (IMN) at Baoji High-Tech Hospital between May 1, 2022, and February 28, 2024. Patients were divided into two groups based on the rituximab (RTX) regimen they received: the standard-dose group (n=157, 375 mg/m<sup>2</sup> regimen) and the low-dose group (n=166, 1 g regimen). The efficacy and safety of these two regimens were compared.

#### *Ethical statement*

The study was approved by the Ethics Committee of Baoji High-Tech Hospital. Informed consent was waived due to the retrospective nature of the study.

#### *Study population*

Inclusion criteria: (1) Patients aged  $\geq 18$  years. (2) Diagnosed with IMN through renal biopsy or positive serum PLA2R antibodies ( $>5$  RU/mL) in the presence of typical nephrotic syndrome (NS) clinical manifestations. (3) A minimum follow-up period of six months and complete clinical data.

Exclusion criteria: (1) Patients with secondary membranous nephropathy (SMN) due to systemic lupus erythematosus (SLE), medications, viral hepatitis, malignancies, or other serious conditions. (2) Patients with severe infections, psychiatric or neurological disorders, severe liver or cardiac dysfunction, or other significant comorbidities.

#### *Treatment regimen*

Patients were assigned to one of two groups based on the RTX regimen administered: The low-dose group received 375 mg/m<sup>2</sup> once every 3 weeks for a total of three doses. The

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standard-dose group received 1 g on days 1 and 15 for a total of two doses. Pre-medications for all patients included intramuscular dexamethasone (5 mg), promethazine (25 mg), oral diphenhydramine (50 mg), and intravenous methylprednisolone succinate to prevent allergic reactions. RTX infusion started at a rate of 25 mL/h, which was gradually increased by 25 mL/h every hour, up to a maximum of 200 mL/h if no adverse reactions occurred.

### *Data source*

Clinical data were extracted from the hospital's electronic medical record system, including:

Baseline information: age, gender, BMI Medical history: diabetes, hypertension, smoking, use of ACE inhibitors/angiotensin receptor blockers (ACEI/ARB).

Laboratory results: serum PLA2R antibodies, urine protein, serum albumin, serum creatinine, IgG, IgA, IgM, C3, C4.

Treatment regimen: administered RTX dosage. Follow-up data: clinical remission rate, adverse reaction rate, and coagulation function parameters (TT, PT, Fib).

### *Detection methods*

Peripheral blood samples (10 mL) were collected at three time points: before treatment, 3 months after treatment, and 6 months after treatment. Five milliliters of each sample were used for routine biochemical tests, while the remaining 5 mL were used for coagulation function testing.

Biochemical tests: Serum PLA2R antibodies, urine protein quantification, serum albumin, and serum creatinine were measured using the Cobas 8000 analyzer (Roche Diagnostics).

Coagulation tests: Thrombin time (TT), prothrombin time (PT), and fibrinogen (Fib) were measured using the CA-7000 automated coagulation analyzer (Sysmex Corporation).

All laboratory procedures adhered to strict quality control standards. Coagulation function data were available only before treatment and at 6 months post-treatment, as some patients did not undergo testing at the 3-month mark.

### *Variable definitions and measurements*

Primary endpoint: Clinical remission rate (including complete and partial remission) following RTX treatment.

Secondary endpoints: Relapse rate, adverse reaction rate, and changes in coagulation function.

Other variables of interest: Patient age, gender, BMI, comorbidities (e.g., diabetes, hypertension), and laboratory parameters (e.g., urine protein, serum albumin, serum creatinine).

### *Statistical analysis*

Data were analyzed using SPSS 20.0 software. Continuous variables were compared between groups using t-tests or rank-sum tests, as appropriate. Categorical variables were analyzed using chi-square tests. Logistic regression models were used to identify factors influencing clinical outcomes, and receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive power of key variables. GraphPad Prism 9 software was used for figure generation. A *P*-value of <0.05 was considered statistically significant.

## **Results**

### *Comparison of baseline data*

As shown in **Table 1**, there were no significant differences in baseline characteristics between the standard-dose and low-dose groups (all *P*>0.05). Specifically, no significant differences were observed in age, gender distribution, BMI, risk level, use of ACE inhibitors/angiotensin receptor blockers (ACEI/ARB), history of diabetes, hypertension, or smoking (all *P*>0.05). Additionally, immunoglobulin levels (IgG, IgA, IgM) and complement components (C3 and C4) were similar between the two groups (all *P*>0.05).

### *Comparison of disease remission rates*

As shown in **Table 2**, no statistically significant differences in disease remission were found between the two groups (*P*>0.05). The complete remission rate was 28.7% (45/157) in the standard-dose group and 31.3% (52/166) in the low-dose group. The overall response rate was 82.2% (129/157) in the standard-dose group and 71.7% (119/166) in the low-dose

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**Table 1.** Comparison of baseline characteristics between groups

Variable	Standard Group (n=157)	Low-Dose Group (n=166)	t/ $\chi^2$ Value	P Value
Age (years)	51.18±10.22	50.82±11.42	0.298	0.766
Gender				
Male	102	101	0.588	0.443
Female	55	65		
BMI	24.00±1.51	24.10±1.65	-0.545	0.586
Risk Level				
High Risk	149	154	0.632	0.427
Medium Risk	8	12		
ACEI/ARB Use				
Yes	75	70	1.024	0.312
No	82	96		
Diabetes History	Yes	16	13	0.55
Hypertension History	Yes	71	61	2.399
Smoking History	Yes	100	105	0.007
IgG (g/L)	5.94±2.54	5.60±2.32	1.25	0.212
IgA (g/L)	1.71±0.51	1.75±0.49	-0.715	0.475
IgM (g/L)	1.08±0.47	1.06±0.49	0.469	0.639
C3 (g/L)	0.89±0.11	0.89±0.16	0.252	0.801
C4 (g/L)	0.25±0.09	0.24±0.08	1.171	0.243

Note: ACEI/ARB: Angiotensin-converting enzyme inhibitors/Angiotensin II receptor blockers, IgG: Immunoglobulin G, IgA: Immunoglobulin A, IgM: Immunoglobulin M, C3: Complement component 3, C4: Complement component 4.

**Table 2.** Comparison of disease remission rates

Group	Complete Remission	Partial Remission	Non-Responsive	Overall Response	Relapse
Standard Group (n=157)	45	80	32	129	30
Low-Dose Group (n=166)	52	67	47	119	32
$\chi^2$ Value	0.272	3.652	3.176	3.176	0.436
P Value	0.602	0.056	0.074	0.074	0.509

group. The relapse rates were 19.1% (30/157) in the standard-dose group and 19.3% (32/166) in the low-dose group. Although the partial remission rate (P=0.056) and non-response rate (P=0.074) approached statistical significance, they did not meet the threshold for significance.

### *Comparison of post-treatment changes in renal function, serum protein, urine protein, and PLA2R*

As depicted in **Figure 1**, no significant differences were observed in changes in 24-hour urine protein, serum albumin, serum creatinine, or PLA2R levels between the standard-dose and low-dose groups before treatment, at three months, and at six months post-treatment (all P>0.05).

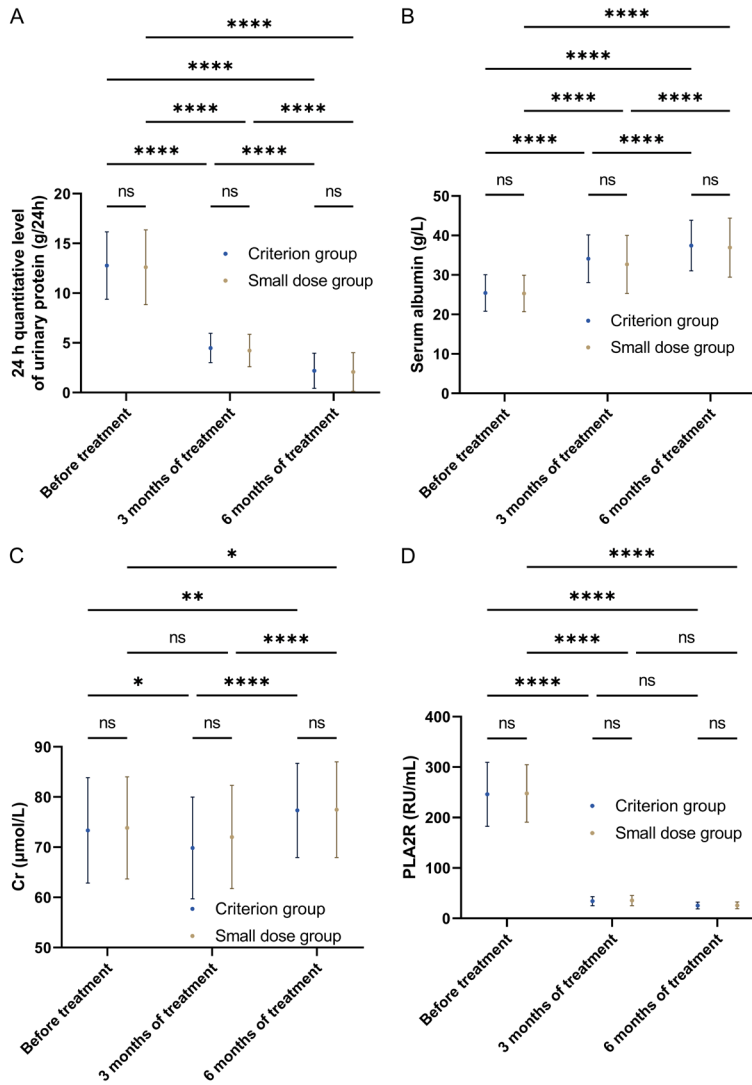
### *Comparison of post-treatment changes in coagulation function*

As shown in **Figure 2**, there were no significant differences in coagulation function indicators between the two groups before treatment and at six months post-treatment (all P>0.05). Specifically, thrombin time (TT, **Figure 2A**), prothrombin time (PT, **Figure 2B**), and fibrinogen (Fib, **Figure 2C**) levels did not differ significantly between the groups, suggesting that the RTX dosage regimens did not significantly affect coagulation function.

### *Comparison of adverse reactions*

As shown in **Table 3**, there were no significant differences in the incidence of adverse reactions between the two groups (all P>0.05). Specifically, the incidence of infections (P=

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**Figure 1.** Comparison of 24-hour urine protein (A), serum albumin (B), creatinine (C), and PLA2R (D) levels between the standard group and the low-dose group before treatment, 3 months after treatment, and 6 months after treatment. ns indicates no statistically significant difference ( $P > 0.05$ ). \* indicates highly statistically significant difference ( $P < 0.05$ ). \*\* indicates very highly statistically significant difference ( $P < 0.01$ ). \*\*\*\* indicates extremely statistically significant difference ( $P < 0.0001$ ). Note: Cr: Creatinine, PLA2R: Phospholipase A2 receptor.

0.501), infusion reactions ( $P = 0.396$ ), liver function impairment ( $P = 0.376$ ), gastrointestinal reactions ( $P = 0.933$ ), hyperglycemia ( $P = 0.288$ ), hypokalemia ( $P = 0.372$ ), and hair loss ( $P = 0.303$ ) were similar between the two groups, with no statistically significant differences.

### Risk factor analysis for coagulation abnormalities

**Table 4** shows significant differences between the hypercoagulability and normal groups in

several variables. The proportion of high-risk patients was significantly higher in the hypercoagulability group ( $P = 0.006$ ). Additionally, the hypercoagulability group exhibited significantly higher levels of diabetes history ( $P < 0.001$ ), hypertension history ( $P < 0.001$ ), age ( $P = 0.043$ ), BMI ( $P < 0.001$ ), 24-hour urine protein at six months post-treatment ( $P < 0.001$ ), and PLA2R levels at six months post-treatment ( $P < 0.001$ ) compared to the normal group. However, no significant differences were observed for gender, ACEI/ARB use, immunoglobulins (IgG, IgA, IgM), complement components (C3, C4), or serum creatinine (all  $P > 0.05$ ).

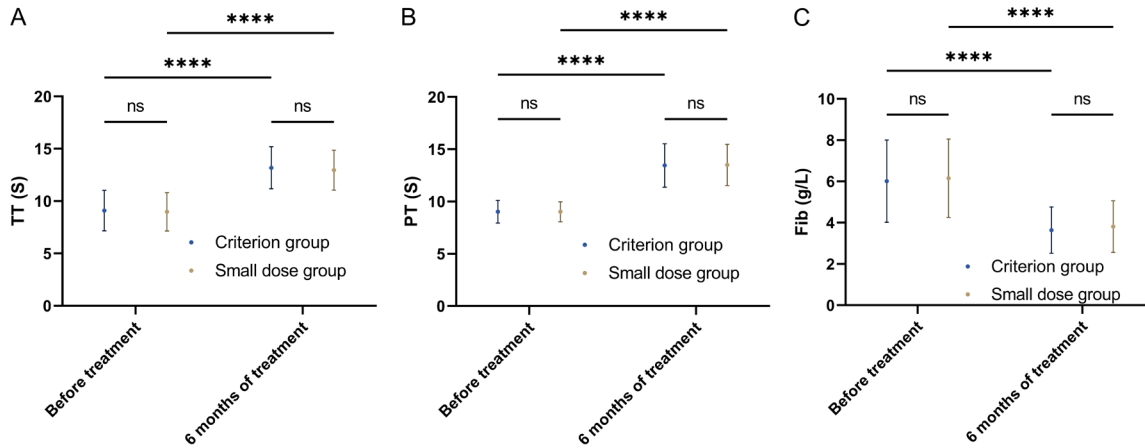
### Multivariate analysis

ROC curve analysis was conducted to determine the optimal cutoff values for continuous variables, which were then dichotomized (**Figure 3** and **Table 5**). Variance inflation factor (VIF) analysis confirmed that all variables had a VIF of less than 2, indicating no multicollinearity (**Table 6**). Forward stepwise regression analysis revealed that BMI (OR=1.710, 95% CI: 1.284-2.339,  $P < 0.001$ ), diabetes history (OR=7.186, 95% CI: 2.118-26.356,  $P = 0.002$ ), 24-hour urine protein at six months post-treatment (OR=2.227, 95% CI: 1.709-3.039,  $P < 0.001$ ), and PLA2R levels at six months post-treatment (OR=1.391, 95% CI: 1.257-1.571,  $P < 0.001$ ) were independent risk factors for hypercoagulability. Age, risk level, and hypertension history did not show statistical significance in the multivariate analysis (**Table 7**).

### Discussion

This study aimed to compare the efficacy and safety of two RTX dosage regimens - 1 g and

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**Figure 2.** Comparison of thrombin time (A), prothrombin time (B), and fibrinogen (C) between the standard group and the low-dose group before treatment and 6 months after treatment. ns indicates no statistically significant difference ( $P > 0.05$ ). \*\*\*\* indicates extremely statistically significant difference ( $P < 0.0001$ ). Note: TT: Thrombin Time, PT: Prothrombin Time, Fib: Fibrinogen.

**Table 3.** Comparison of adverse reactions

Variable	Standard Group (n=157)	Low-Dose Group (n=166)	$\chi^2$ Value	P Value
Infection	41	38	0.454	0.501
Infusion Reaction	7	11	0.721	0.396
Liver Function Impairment	20	16	0.783	0.376
Gastrointestinal Reaction	25	27	0.007	0.933
Hyperglycemia	3	1	1.129	0.288
Hypokalemia	4	2	0.798	0.372
Hair Loss	1	0	1.061	0.303

375 mg/m<sup>2</sup> - in patients with IMN and to assess their effects on coagulation function. The results showed no significant differences between the two regimens in terms of disease remission rates, relapse rates, or adverse reactions, suggesting that the 1 g regimen may be as effective and safe as the standard 375 mg/m<sup>2</sup> regimen for treating IMN.

In terms of efficacy, the complete remission rate was 28.7% in the standard-dose group and 31.3% in the low-dose group, with overall response rates of 82.2% and 71.7%, respectively. These findings align with previous studies highlighting the effectiveness of RTX in treating IMN. For instance, Dahan et al. emphasized RTX's efficacy in patients with severe membranous nephropathy and the role of PLA2R levels in evaluating treatment response [20]. Similarly, Maharjan et al. demonstrated that B-cell depletion therapy significantly reduces proteinuria and enhances clinical remission rates [21]. Although no significant differences were ob-

served in this study, the partial remission rate approached significance, suggesting that larger-scale studies may uncover potential differences between the two dosage regimens.

Other studies have suggested that RTX dosage may influence treatment outcomes. Li et al. proposed that higher doses of RTX might be more effective in certain subgroups, particularly in those with high PLA2R antibody levels [22]. As research on RTX's mechanisms continues, studies have shown that changes in anti-PLA2R antibody levels are closely associated with treatment responses. Cravedi et al. demonstrated a significant correlation between decreased anti-PLA2R antibody levels and clinical remission, suggesting that monitoring these antibodies could help predict treatment outcomes and guide clinical decision-making [23].

This study found no significant effect of RTX dosage on coagulation parameters, including TT, PT, and Fib, both before treatment and six

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**Table 4.** Comparison of baseline characteristics between the hypercoagulable and normal groups

Variable	Hypercoagulable Group (n=67)	Normal Group (n=256)	t/ $\chi^2$ Value	P Value
Treatment Regimen			3.251	0.071
Standard Group	26	131		
Low-Dose Group	41	125		
Age (years)	51.18±10.22	50.82±11.42	0.298	0.766
Gender			0.064	0.8
Male	43	160		
Female	24	96		
BMI	24.00±1.51	24.10±1.65	-0.545	0.586
Risk Level			7.631	0.006
High Risk	58	245		
Medium Risk	9	11		
ACEI/ARB Use			1.962	0.161
Diabetes History	Yes	19	10	38.851
Hypertension History	Yes	41	91	14.454
Smoking History	Yes	40	165	0.517
Treatment Efficacy			1.626	0.444
Complete Remission	17	80		
Partial Remission	30	117		
Non-Responsive	20	59		
Age (years)	53.43±11.01	50.36±10.72	2.048	0.043
BMI (kg/m <sup>2</sup> )	25.01±1.53	23.80±1.50	5.815	<0.001
IgG (g/L)	5.82±2.55	5.75±2.41	0.2	0.842
IgA (g/L)	1.79±0.44	1.71±0.51	1.316	0.191
IgM (g/L)	1.04±0.48	1.07±0.48	-0.46	0.646
C3 (g/L)	0.90±0.15	0.89±0.14	0.501	0.618
C4 (g/L)	0.25±0.07	0.24±0.09	0.993	0.322
24-Hour Urine Protein (g/24 h, 6 months)	3.72±1.73	1.21 [0.22, 2.78]	7.483	<0.001
Serum Albumin (g/L, 6 months)	36.64±6.92	38.00 [33.00, 42.00]	-1.052	0.292
Creatinine ( $\mu$ mol/L, 6 months)	77.50±10.45	77.39±9.18	0.077	0.939
PLA2R (RU/mL, 6 months)	30.92 [28.02, 35.47]	23.96±5.97	8.557	<0.001

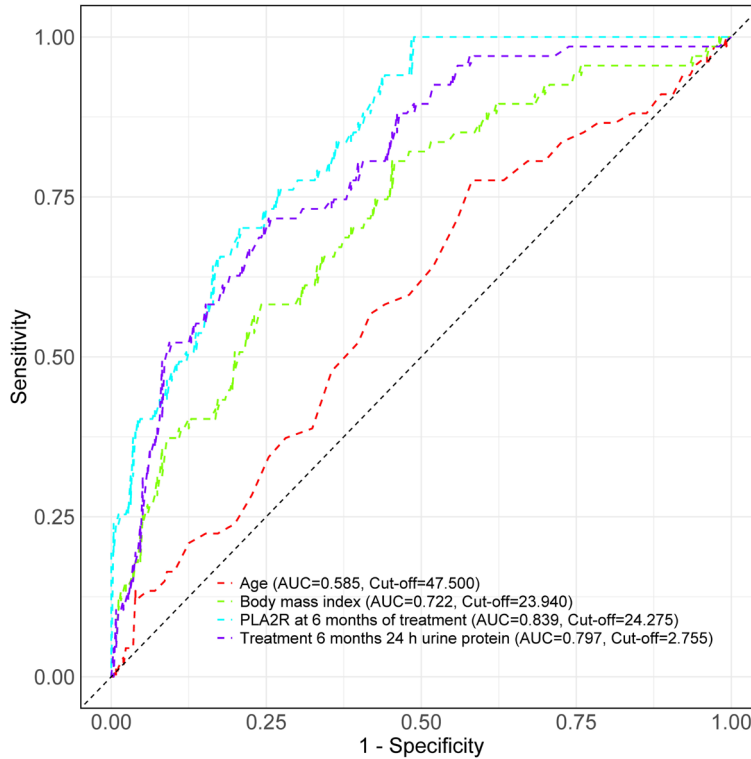
Note: ACEI/ARB: Angiotensin-converting enzyme inhibitors/Angiotensin II receptor blockers, IgG: Immunoglobulin G, IgA: Immunoglobulin A, IgM: Immunoglobulin M, C3: Complement component 3, C4: Complement component 4, Cr: Creatinine, PLA2R: Phospholipase A2 receptor, BMI: body mass index.

months post-treatment. This lack of significant change may be attributed to pre-existing coagulation abnormalities in IMN patients, particularly those with nephrotic syndrome. It is well established that IMN, especially in the context of nephrotic syndrome, is associated with hypoalbuminemia and hyperlipidemia, both of which contribute to a hypercoagulable state. Despite the immunosuppressive effects of RTX, these underlying conditions were not significantly altered by treatment [24].

Previous studies have suggested that coagulation abnormalities in nephrotic syndrome arise

from physiological changes, such as increased synthesis of coagulation factors by the liver and alterations in plasma proteins [25]. The relationship between hypercoagulability and IMN should not be underestimated, as patients with severe proteinuria and hypoalbuminemia are at an increased risk for thrombotic events, including deep vein thrombosis and pulmonary embolism. Sanjeev Kumar et al. reported a strong association between severe proteinuria and thrombosis in IMN patients, highlighting the importance of closely monitoring proteinuria levels [26].

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**Figure 3.** ROC curve analysis for age, BMI, PLA2R levels at 6 months, and 24-hour urine protein. BMI: body mass index, PLA2R: phospholipase A2 receptor.

**Table 5.** Assignment table for variables

Variable	Assignment
Age (years)	$\geq 45=1$ , $<45=0$
BMI (kg/m <sup>2</sup> )	$\geq 23.94=1$ , $<23.94=0$
Risk Level	High Risk =1, Medium Risk =0
Diabetes History	Yes =1, No =0
Hypertension History	Yes =1, No =0
24-Hour Urine Protein (6 months)	$\geq 24.275=1$ , $<24.275=0$
PLA2R (6 months)	$\geq 2.755=1$ , $<2.755=0$

Note: BMI: body mass index, PLA2R: Phospholipase A2 receptor.

**Table 6.** Variance inflation factor (VIF)

Variable	VIF
Age	1.0172
BMI	1.1036
Risk Level	1.0854
Diabetes History	1.091
Hypertension History	1.0301
24-Hour Urine Protein (6 months)	1.3822
PLA2R (6 months)	1.4488

Note: BMI: body mass index, PLA2R: Phospholipase A2 receptor.

Our study identified several independent risk factors for hypercoagulability, including BMI, diabetes history, 24-hour urine protein levels at six months post-treatment, and PLA2R levels. A higher BMI is often linked to systemic inflammation and metabolic disturbances, which promote the synthesis of coagulation factors [27]. Diabetes contributes to a hypercoagulable state through mechanisms such as enhanced platelet activation, increased fibrinogen production, and inhibition of fibrinolysis [28]. Increased proteinuria serves as a marker of more severe renal injury, indicating glomerular and tubular damage, which may further impair coagulation function [29]. Additionally, elevated PLA2R levels - an important biomarker in membranous nephropathy - are associated with disease activity and have been linked to hypercoagulability [25]. Elevated PLA2R levels likely reflect a more robust immune response, potentially further influencing coagulation status. Therefore, in clinical practice, it is crucial to consider these risk factors (e.g., proteinuria, PLA2R levels, etc.) when monitoring coagulation function in IMN patients.

Regarding safety, the incidence of adverse reactions did not differ significantly between the two groups, consistent with previous studies reporting favorable safety profiles for RTX. Zonozi et al. [30] noted that RTX, when used in combination with other immunosuppressive therapies, has a good safety profile. Our study supports these findings, particularly regarding infections and infusion reactions, which are the most commonly reported adverse effects. The infection rates observed in this study were similar to those reported in prior studies, indicating that RTX's infection risk remains relatively manage-



**Table 7.** Multivariate analysis

Variable	Estimate	Std Error	P Value	OR	Lower	Upper
Age	0.015	0.018	0.393	1.015	0.98	1.052
BMI	0.537	0.152	<0.001	1.71	1.284	2.339
Risk Level	1.164	0.755	0.123	3.202	0.698	13.99
Diabetes History	1.972	0.636	0.002	7.186	2.118	26.356
Hypertension History	0.452	0.426	0.288	1.571	0.679	3.641
24-Hour Urine Protein (6 months)	0.801	0.146	<0.001	2.227	1.709	3.039
PLA2R (6 months)	0.33	0.057	<0.001	1.391	1.257	1.571

Note: BMI: body mass index, PLA2R: Phospholipase A2 receptor.

able. However, while RTX generally demonstrates a favorable safety profile, some patients may still experience serious adverse events, such as infusion-related reactions or liver function impairment. This underscores the importance of closely monitoring clinical and laboratory parameters during RTX treatment to promptly detect and manage any adverse events.

In conclusion, this study compared the efficacy and safety of 1 g and 375 mg/m<sup>2</sup> RTX dosages in patients with IMN and found no significant differences between the two regimens in terms of clinical remission rates, relapse rates, or adverse reactions, with both regimens demonstrating acceptable safety profiles. The study also identified several independent risk factors for hypercoagulability, including BMI, diabetes history, 24-hour urine protein levels at six months post-treatment, and PLA2R levels. These findings provide valuable evidence for optimizing the treatment of IMN and support the flexible use of RTX dosage regimens based on individual patient characteristics in clinical practice.

**Disclosure of conflict of interest**

None.

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