

# A Single-Center, Cross-Sectional Study of Children with Steroid-Resistant Nephrotic Syndrome in Southern China

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**Introduction.** We conducted a cross-sectional study on children with steroid-resistant nephrotic syndrome (SRNS) in a single center in Southern China.

**Methods.** A total of 166 SRNS cases in the Paediatric Nephrology Center of the First Affiliated Hospital of Sun Yat-Sen University from September 1, 2006, to August 31, 2016 were retrospectively analysed. The inclusion criteria were: 1) age  $\leq$  14 years, 2) diagnosed with SRNS, and 3) without purpura nephritis, immunoglobulin A nephropathy, lupus nephritis, or another secondary nephritis. Incidences of primary/late steroid-resistance and curative effects were analysed.

**Results.** The median follow-up time was 4.64 (2.64 to 8.11) years. There were 67 cases of complete remission (CR) (40.36%), 46 cases of partial remission (PR) (27.71%), 31 cases of no remission (NR) (18.67%), 18 cases of end-stage renal disease (ESRD, 10.84%, including 7 cases of kidney transplantation), and 4 cases of death due to hematoma and severe infection after renal biopsy; renal failure after progression to ESRD; sepsis during glucocorticoid (GC) + Cyclosporine A (CsA) treatment; and multiple organ failure at the onset of disease, respectively. For the 8 cases with gene mutation, unnecessary drug treatment should be reduced due to their low responsiveness to immunosuppressive treatment. Female, patients with hematuria, primary steroid-resistance (PSR) type and histopathologic focal segmental glomerulosclerosis (FSGS) were more likely to have higher ESRD rate. Subgroup analysis of ESRD suggested that female patients and patients with PSR type were more likely to develop ESRD. Cox-regression analysis showed that female (HR = 3.04, 95% CI: 1.18 to 7.86;  $P < .05$ ), without hematuria (HR = 0.36, 95% CI: 0.14 to 0.91;  $P < .05$ ), and LSR type (HR = 0.17, 95% CI: 0.04 to 0.74;  $P < .05$ ) were significantly associated with ESRD. Kaplan-Meier survival analysis also showed the same trends.

**Conclusion.** Of the 166 SRNS cases, 68.07% of patients achieved CR or PR, 18.67% of cases had NR, 10.84% of cases developed ESRD, and 2.41% of patients died during follow-up. Female gender, hematuria, and PSR type were positively associated with ESRD.

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## INTRODUCTION

Nephrotic syndrome (NS) is defined as the occurrence of proteinuria, hypoalbuminemia, edema, and hyperlipidemia.<sup>1</sup> According to the responsiveness to steroid therapy, NS can be

divided into steroid-sensitive nephrotic syndrome (SSNS), steroid-dependent nephrotic syndrome (SDNS) and steroid-resistant nephrotic syndrome (SRNS).<sup>2</sup> SRNS is defined as a failure of remission following 4 weeks daily corticosteroid therapy in

NS patients.<sup>3</sup> The incidence of SRNS is gradually increasing,<sup>4</sup> accounting for nearly 15 ~ 30% of all NS cases.<sup>4,5</sup>

Immunosuppressive drugs, such as calcineurin inhibitors, cyclosporine and tacrolimus, are the standard treatments for SRNS.<sup>6</sup> The long-term outcome of SRNS in children includes complete remission (CR), partial remission (PR), no remission (NR) and end-stage renal disease (ESRD).<sup>7</sup> With the advancement in treatment technologies, approximately 80% of SRNS cases are steroid-responsive and have a favorable prognosis.<sup>8</sup> However, a small fraction of SRNS cases still progress to end-stage renal disease (ESRD) within 10 years.<sup>9,10</sup>

Current studies on Chinese SRNS patients mainly focus on the efficacy of drug treatment<sup>11-13</sup> and genetic analysis of SRNS patients.<sup>14-16</sup> There is no study on risk factors for developing ESRD in Chinese patients with SRNS. In this study, we conducted a cross-sectional analysis on children with SRNS in a single hospital of Guangdong, Southern China.

## MATERIALS AND METHODS

### Study Subjects

This was a retrospective cross-sectional study including 166 SRNS patients hospitalized in the Paediatric Nephrology Center of the First Affiliated Hospital of Sun Yat-Sen University from September 1, 2006, to August 31, 2016. The inclusion criteria were: 1) age  $\leq$  14 years, 2) diagnosed with nephrotic syndrome,<sup>17</sup> 3) clinical diagnosis of SRNS, which was defined as positive urinary protein after 4 weeks of treatment with sufficient steroid doses (2 mg/kg/d or 60 mg/m<sup>2</sup>/d),<sup>18</sup> 4) with complete data, and 5) without diagnosis of purpura nephritis, immunoglobulin A nephropathy, lupus nephritis, or another secondary nephritis.

### Definitions

In our hospital, NS is divided into primary NS (PNS), secondary NS (SNS) and congenital NS (CNS) according to the causes of disease. According to the responsiveness to steroid therapy, NS can be divided into SSNS, SDNS and SRNS. The SRNS can be further divided into primary steroid-resistance (PSR) and late steroid-resistance (LSR) based on the timing of steroid-resistance. The PSR was defined as the failure of remission during the initial 4 weeks

of daily steroid therapy (2 mg/kg/d or 60 mg/m<sup>2</sup>/d), while LSR was defined as unresponsiveness to 4 weeks of daily steroid therapy (2 mg/kg/d or 60 mg/m<sup>2</sup>/d) in a patient whose condition was previously steroid-sensitive.

Hypertension was defined as exceeding the 95<sup>th</sup> percentile for systolic or diastolic blood pressure for age, sex, and height. Haematuria was determined by the presence of more than ten red blood cells per high power field.

The treatment outcome of SRNS was assessed as follows:<sup>18</sup> Complete remission (CR) was defined as normal blood biochemistry and urine test. Partial remission (PR) was defined as positive for urinary protein ( $\leq$  ++ ) and/or disappearance of edema and plasma albumin greater than 2.5 g/L. No remission (NR) was defined as positive for urinary protein ( $\geq$  ++). ESRD was defined as an endogenous creatinine clearance rate (Ccr) of less than 10 mL/min  $\times$  1.73m<sup>2</sup> and requiring dialysis or renal transplantation. The creatinine clearance was calculated according to the following formula:<sup>19</sup>

$$\text{Ccr (mL/min} \times 1.73\text{m}^2) = \frac{[24\text{-h urine creatinine } (\mu\text{mol}) / \text{serum creatinine } (\mu\text{mol/mL})] \times \{1.73\text{m}^2 / [(24 \times 60 \text{ (min)}) \times \text{body surface area (m}^2)]\}}{}$$

The effective cases were defined as complete or partial remission. The non-responders were defined as without remission, ESRD, or death.

### Therapy

Cyclosporine A (CsA) therapy:<sup>20</sup> 4 to 6 mg/kg/d or 100 to 150 mg/m<sup>2</sup>/d and once every 12 hours to maintain a serum trough level of 80 to 120  $\mu$ g/L.

Tacrolimus (TAC) therapy:<sup>21</sup> 0.1 to 0.15 mg/kg/d once every 12 hours to maintain a serum trough level of 5 to 10 ng/mL.

The 2016 China SRNS guideline recommends cyclophosphamide as one of the treatment drugs for SRNS.<sup>22</sup> Cyclophosphamide (CTX) therapy: 8 to 12 mg/kg/d was administered through an intravenous drip 2 days every 2 weeks; the total accumulated dose should not exceed 168 mg/kg.<sup>18</sup>

The medications for genetically approved SRNS were TAC or CsA.

### Renal Biopsy

- 1) Puncture Method: A Bard puncture gun was used to create a puncture under the real-time guidance of a B-ultrasonic detection system.
- 2) Routine optical microscopy, electron microscopy,

and immunofluorescence were performed on the renal biopsy.

- 3) According to the World Health Organization revised classification criteria of 1995<sup>23</sup> for glomerular disease, pathological findings included focal segmental glomerulosclerosis (FSGS), minimal change disease (MCD), mesangial proliferative glomerulonephritis (MsPGN), membranoproliferative glomerulonephritis (MPGN) and membranous nephropathy (MN).

### Genetic Analysis

Genetic Analysis is important for SRNS.<sup>24</sup> In this study, polymerase chain reaction amplification and DNA sequencing of two generations were applied. In 11 cases, 27 to 162 target genes, including *NPHS2*, *NPHS1*, *WT1*, *MYO1E*, and *INF2*, were detected by a panel.

### Data Collection

Demographic and clinical data of all children and gene detection results of the 11 cases were collected and analysed from the patients' medical records, including age, sex, blood pressure, treatment, prognosis, 24-hour urinary protein concentration, serum albumin, serum creatinine, and routine urine and other laboratory tests.

### Statistical Analysis

Continuous variables were reported with mean  $\pm$  standard deviation (SD) and were compared using Student's independent t-test or Mann-Whitney U test (if normality was not assumed). One-way ANOVA test and Fisher's LSD test as post-hoc comparison were used to compare means among groups (more than 2). Categorical variables were presented as number and percentage and were compared using the Chi-square test or Fisher's exact test (if expected value  $\leq 5$  was found). To further investigate the association between independent variables and ESRD (excluding death cases), survival analyses were used, including Cox proportional-hazards regression model and Kaplan-Meier survival analysis. All analyses were done using IBM SPSS Version 25. The statistical significance level for all the tests was set at a  $P < .05$ , two-tailed.

### Ethical Considerations

The study was approved by the ethics committee of the First Affiliated Hospital of Sun Yat-sen

University for retrospective analysis (approval no. [2016] 209). Written consent was provided by each patient's parents or guardians before the renal biopsy and genetic tests.

## RESULTS

### Patient's Clinical Characteristics

As shown in Figure 1, 166 SRNS patients were included in this study. The follow-up period ranged from 0.35 to 10 years, the median (IQR) was 4.64 (2.64 to 8.11) years. There were 67 cases of CR (40.36%), 46 cases of PR (27.71%), and 53 cases of NR (31.93%). Of the NR cases, 18 cases ended up with ESRD (33.96%) (including 7 cases of renal transplantation), and 4 cases of death (7.55%) due to hematoma and severe infection after renal biopsy; renal failure after progression to ESRD; sepsis during glucocorticoid (GC) + CsA therapy; and multiple organ failure at the onset of disease, respectively. Progression to ESRD took an average of  $4.66 \pm 2.29$  years.

### Comparison of Characteristics Among Different Outcome Subgroups

As shown in Table 1, patient's demographic and

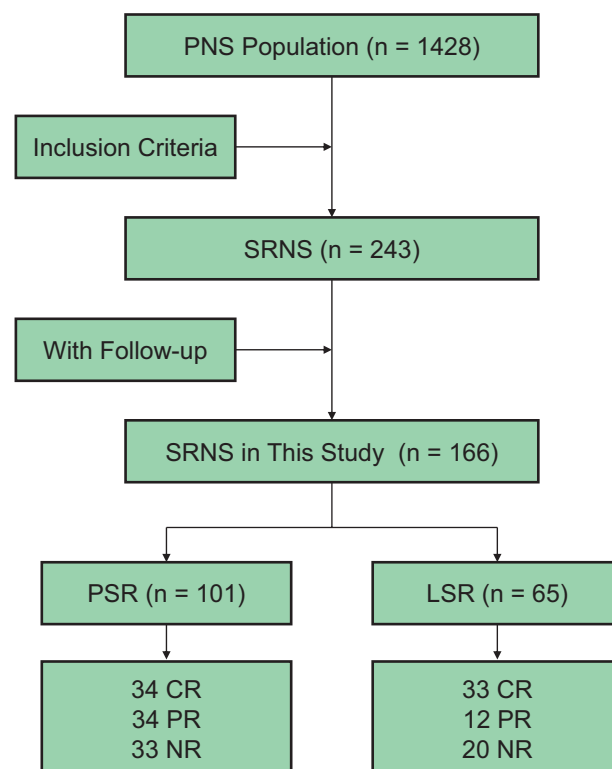


Figure 1. The Flow Chart of Enrolled Cases

**Table 1.** Relations Between Patient's Demographic and Clinical Characteristics and Prognosis in Children with SRNS

Parameters (# of case)	Prognosis (%)			P
	CR (n = 67)	PR (n = 46)	NR (n = 53)	
Age, year	4.54 ± 3.29	5.42 ± 3.31	4.65 ± 3.27	> .05
Gender				
Male (107)	50 (46.73%)	30 (28.04%)	27 (25.23%)	< .05
Female (59)	17 (28.81%)	16 (27.12%)	26 (44.07%)	
Clinical Type				
Simple (110)	56 (50.91%)	25 (22.73%)	29 (26.36%)	< .05
Nephritis (56)	11 (19.64%)	21 (37.50%)	24 (42.86%)	
Hypertension				
Yes (5)	2 (40.00%)	0 (0.00%)	3 (60.00%)	> .05
No (161)	65 (40.37%)	46 (28.57%)	50 (31.06%)	
Hematuria				
Yes (47)	8 (17.02%)	20 (42.55%)	19 (40.43%)	< .001
No (119)	59 (49.58%)	26 (21.85%)	34 (28.57%)	
Initial Steroid Responsiveness				
PSR (101)	34 (33.66%)	34 (33.66%)	33 (32.67%)	< .05
LSR (65)	33 (50.77%)	12 (18.46%)	20 (30.77%)	
Histopathologic Diagnosis				
MCD (44)	27 (61.36%)	10 (22.73%)	7 (15.91%)	< .05
FSGS (62)	17 (27.42%)	18 (29.03%)	27 (43.55%)	
MsPGN (25)	10 (40.00%)	5 (20.00%)	10 (40.00%)	
MPGN (5)	1 (20.00%)	3 (60.00%)	1 (20.00%)	
MN (4)	0 (0.00%)	2 (50.00%)	2 (50.00%)	
CsGN (2)	0 (0.00%)	2 (100.00%)	0 (0.00%)	
DMS (1)	0 (0.00%)	0 (0.00%)	1 (100.00%)	
Therapeutic Method				
CTX (25)	9 (36.00%)	5 (20.00%)	11 (44.00%)	> .05
CNIs (112)	56 (48.70%)	34 (29.57%)	25 (21.74%)	
Plasma-albumin, g/L	19.72 ± 7.21	21.12 ± 8.95	20.63 ± 7.83	> .05
Cholesterol, mmol/L	12.58 ± 4.24	10.81 ± 4.49	12.66 ± 4.11	> .05
Urine Protein Quantitation, mg/kg × d	123.30 ± 96.07	144.21 ± 113.59	145.01 ± 97.83	> .05
Endogenous Ccr, mL/min × 1.73 m <sup>2</sup>	114.39 ± 53.50	123.42 ± 57.07	109.72 ± 56.10	> .05
Gene Mutation or Not				
No Gene Mutation (16)	4 (25.00%)	3 (18.75%)	9 (56.25%)	> .05
Gene Mutation (8)	1 (12.50%)	1 (12.50%)	6 (75.00%)	
ESRD				
Yes (18)	0 (0.00%)	0 (0.00%)	18 (100.00%)	< .001
No (148)	67 (45.27%)	46 (31.08%)	35 (23.65%)	
Death				
Yes (4)	0 (0.00%)	0 (0.00%)	4 (100.00%)	< .05
No (162)	67 (41.36%)	46 (28.40%)	49 (30.25%)	

Abbreviations: CR, complete remission; PR, partial remission; NR, no remission; ESRD, end-stage renal disease; PSR, primary steroid-resistance; LSR, late steroid-resistance; FSGS, focal segmental glomerulosclerosis; MCD, minimal change diseases; MsPGN, mesangial proliferative glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MN, membranous nephropathy; SGN, sclerosing glomerulonephritis; DMS, diffuse mesangial sclerosis; CTX, cyclophosphamide; TAC, tacrolimus; CsA, cyclosporine A.

clinical characteristics were compared among the different outcome subgroups (CR, PR, and NR). Significant differences were found in gender, clinical type, hematuria history, initial steroid responsiveness type, histopathologic diagnosis, ESRD and death cases (all  $P < .05$ ). It seems that female cases, nephritis type, with hematuria, PSR

type, and FSGS in histopathology were more likely to have higher NR rates. No significant differences were found in other independent variables (all  $P > .05$ ).

Gene detection was carried out in 24 children with PSR, and 8 cases (33.33%) had gene mutations, with an average age of onset of 5.6 years. The main

resistance genes were NPHS2 (3 cases), NPHS1 (2 cases), INF2 (2 cases), and MYO1E (1 case). The main pathological type was FSGS. In the 8 FSGS cases, 2 had NR, and 4 had ESRD. In the 8 cases with gene mutation, drug treatments were effective in 2 cases and ineffective in 6 cases. In the 16 cases with no gene mutation, in 9 cases were effective, and 7 cases were ineffective. The prognosis difference was not statistically significant ( $P > .05$ ).

### Comparison Between Non-ESRD and ESRD Patients

Among the 166 cases, 162 survived, including 18 cases of ESRD and 144 cases of non-ESRD. The patient's characteristics were compared between these two subgroups. Similar to previous comparisons, the female patients, PSR type were more likely to have ESRD (all  $P < .05$ , Table 2).

### Association Between Independent Variables and ESRD

To further investigate the association between independent variables and ESRD (excluding death cases), survival analyses were performed, including Cox proportional-hazards regression model and Kaplan-Meier survival analysis. As shown in Table 3, female patients (HR = 3.04, 95% CI: 1.18 to 7.86;  $P < .05$ ), without hematuria (HR = 0.36, 95% CI: 0.14 to 0.91;  $P < .05$ ), and LSR type (HR = 0.17, 95% CI: 0.04 to 0.74;  $P < .05$ ) were significantly associated with ESRD. Female patients, with hematuria, and PSR type were positively associated with ESRD. Kaplan-Meier survival functions (Figure 2) indicated the same trends.

### DISCUSSION

In this study, we investigated the outcome of

**Table 2.** Univariate Analysis of ESRD in Children with SRNS

Parameters (# of case)	Non-ESRD (n = 144)	ESRD (n = 18)	P
Age, year	4.93 ± 3.25	3.60 ± 3.19	> .05
Gender			
Male (107)	99 (93.40%)	7 (6.60%)	< .05
Female (59)	45 (80.36%)	11 (19.64%)	
Hypertension			
Yes (5)	4 (80.00%)	1 (20.00%)	> .05
No (161)	140 (89.17%)	17 (10.83%)	
Hematuria			
Yes (47)	38 (82.61%)	8 (17.39%)	> .05
No (119)	106 (91.38%)	10 (8.62%)	
Initial Steroid Responsiveness			
PSR (101)	82 (83.67%)	16 (16.33%)	< .05
LSR (65)	62 (96.88%)	2 (3.13%)	
Histopathologic Diagnosis			
MCD (44)	43 (97.73%)	1 (2.27%)	> .05
FSGS (62)	48 (80.00%)	12 (20.00%)	
MsPGN (25)	22 (91.67%)	2 (8.33%)	
MPGN (5)	5 (100.00%)	0 (0.00%)	
MN (4)	4 (100.00%)	0 (0.00%)	
SGN (2)	2 (100.00%)	0 (0.00%)	
DMS (1)	1 (100.00%)	0 (0.00%)	
Therapeutic Method			
CTX (25)	22 (88.00%)	3 (12.00%)	> .05
CNIs (112)	98 (87.50%)	14 (12.50%)	
Plasma-albumin, g/L	20.36 ± 8.02	19.99 ± 7.46	0.853
Cholesterol, mmol/L	12.08 ± 4.27	12.49 ± 4.79	0.704
Urine Protein Quantitation, mg/kg × d	134.11 ± 101.84	143.78 ± 107.82	0.745
Endogenous Ccr, mL/min × 1.73 m <sup>2</sup>	113.66 ± 52.98	131.68 ± 72.83	0.288

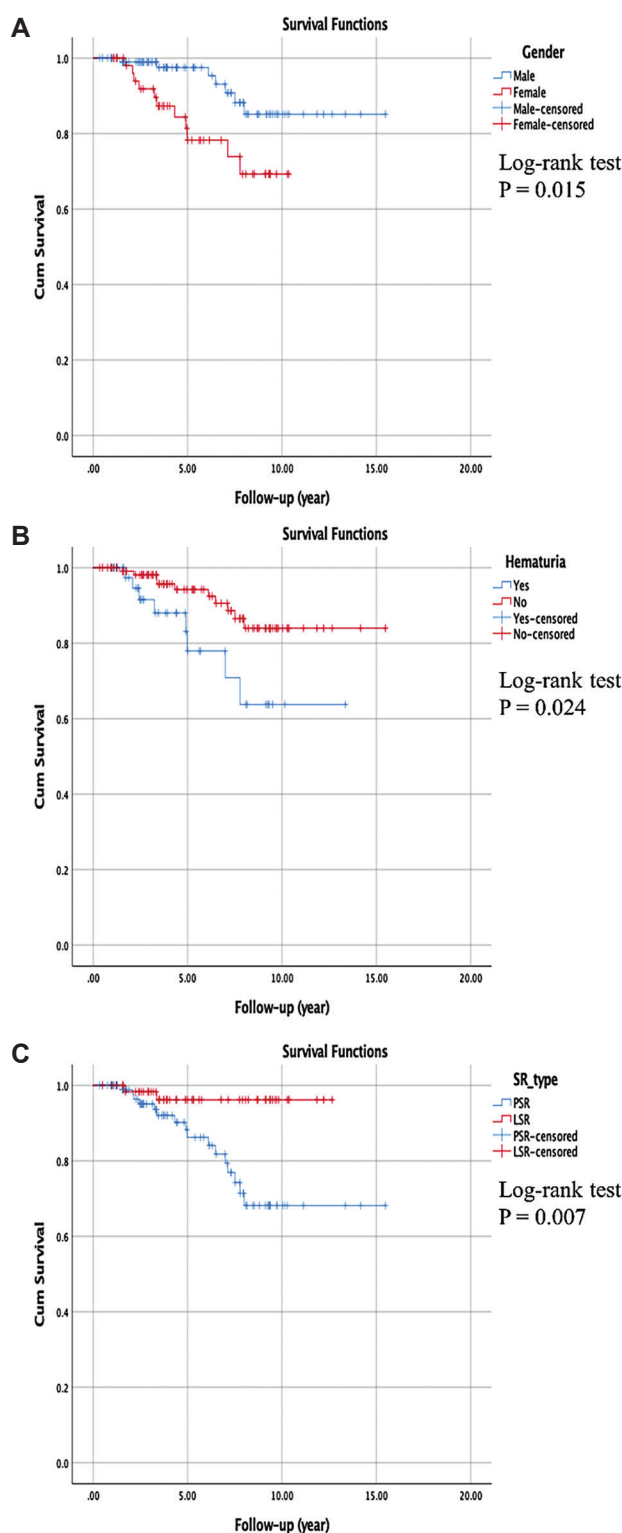
Abbreviations: ESRD, end-stage renal disease; PSR, primary steroid-resistance; LSR, late steroid-resistance; FSGS, focal segmental glomerulosclerosis; MCD, minimal change diseases; MsPGN, mesangial proliferative glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MN, membranous nephropathy; SGN, sclerosing glomerulonephritis; DMS, diffuse mesangial sclerosis; CNIs, calcineurin inhibitors; CTX, cyclophosphamide.

**Table 3.** Cox Proportional-hazards Regression Model Results Between Independent Variables and ESRD

Parameters	HR (95% CI)	P
Age, year	0.86 (0.72 to 1.04)	> .05
Gender		
Male	ref.	-
Female	3.04 (1.18 to 7.86)	< .05
Hypertension		
Yes	ref.	-
No	0.71 (0.09 to 5.35)	> .05
Hematuria		
Yes	ref.	-
No	0.36 (0.14 to 0.91)	< .05
Initial Steroid Responsiveness		
PSR	ref.	-
LSR	0.17 (0.04 to 0.74)	< .05
Histopathologic Diagnosis		> .05
MCD	ref.	-
FSGS	13.42 (1.73 to 104.22)	< .05
MsPGN	4.77 (0.43 to 52.77)	> .05
MPGN	failed estimation	> .05
MN	failed estimation	> .05
SGN	failed estimation	> .05
DMS	failed estimation	> .05
Therapeutic Method		> .05
CTX	ref.	-
CNIs	1.12 (0.32 to 3.90)	> .05
Plasma-albumin, g/L	1.00 (0.94 to 1.07)	> .05
Cholesterol, mmol/L	1.01 (0.90 to 1.13)	> .05
Urine Protein Quantitation, mg/kg × d	1.00 (1.00 to 1.01)	> .05
Endogenous Ccr, mL/min × 1.73 m <sup>2</sup>	1.01 (1.00 to 1.02)	> .05

Abbreviations: ESRD, end-stage renal disease; PSR, primary steroid-resistance; LSR, late steroid-resistance; FSGS, focal segmental glomerulosclerosis; MCD, minimal change diseases; MsPGN, mesangial proliferative glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MN, membranous nephropathy; SGN, sclerosing glomerulonephritis; DMS, diffuse mesangial sclerosis; CNIs, calcineurin inhibitors; CTX, cyclophosphamide.

SRNS and independent factors associated with ESRD by retrospectively analyzing 166 SRNS cases. The results showed that within a median follow-up duration of 4.64 years, there were 40.36% cases of CR, 27.71% cases of PR, 18.67% cases of NR, 10.84% cases of ESRD, and 2.41% cases of death. Comparison among the different outcome subgroups showed that female cases, hematuria, PSR type, and histopathologic FSGS were more likely to have higher ESRD rates. The proportions of female gender and PSR type were significantly higher in the ESRD group than in the non-ESRD group (both  $P < .05$ ). Cox proportional-hazards regression model analysis revealed that female patients, with hematuria, and



**Figure 2.** Kaplan-Meier Survival Function of Independent Variables to ESRD, Including Gender (A), Initial Steroid Responsiveness (B), and Hematuria (C).

PSR type were significantly associated with ESRD. Kaplan-Meier survival analysis also demonstrated

that females, patients with hematuria, and PSR type had a higher incidence of ESRD as compared with males, patients without hematuria, and LSR type.

According to the treatment outcomes of SRNS, effective cases are defined as the patients achieving CR or PR after treatment, while the ineffective cases are those with NR, ESRD, or death.<sup>25</sup> According to previous studies, the effective rate of SRNS ranges from 56.6% to 92.3%.<sup>7,26,27</sup> In China, Chen *et al.* reported that the effective rate of SRNS for children in a Chongqing single center was 79.0%,<sup>28</sup> while Huang *et al.* showed that the effective rate of SRNS in a Shanghai single center was 80.2%.<sup>29</sup> In this study, the effective rate of SRNS was 68.1%, which may be due to the large time span (10 years) and long follow-up duration (the median time = 4.64 years) in the current study.

The histopathologic types of renal biopsy play an important role in the prognosis of SRNS.<sup>7</sup> In this study, FSGS was the most common histopathological type in SRNS,<sup>30</sup> accounting for 43.4% of all SRNS cases. It has been reported that SRNS patients with FSGS have a worse prognosis and a higher risk for developing ESRD<sup>31,32</sup> than other histopathologic types. It has been reported that FSGS is a risk factor for ESRD in SRNS patients.<sup>7,33</sup> In this study, the incidence of FSGS was higher in patients with ESRD as compared with other outcome groups. However, FSGS was not a significant independent factor for ESRD in SRNS patients in our Cox proportional-hazards regression model and Kaplan-Meier survival analyses.

According to the timing of steroid-resistance, SRNS can be divided into PSR and LSR. It has been reported that patients with LSR usually have a good responsiveness to GC therapy combined with immunosuppressive agents and have a good prognosis.<sup>34</sup> Patients with LSR have a better outcome than those with PSR.<sup>10,33,35</sup> In this study, the ESRD rate was higher in PSR cases than in LSR cases (15.84% vs. 3.08%). Likewise, the ESRD patients had a significantly higher rate of PSR than non-ESRD patients (16.33% vs. 3.13%,  $P < .05$ ). Moreover, Cox proportional-hazards regression analysis demonstrated that patients with PSR had a 5.9 times higher risk for developing ESRD as compared with those with LSR. These findings are consistent with Zagury *et al.*'s report.<sup>33</sup>

For SRNS children with gene mutation, unnecessary drug treatment should be reduced due

to their low responsiveness to immunosuppressive agents.<sup>25</sup> Among the 8 SRNS cases with gene mutation in this study, only two cases treated with CsA or TAC could achieve CR and PR. Other 6 patients mainly were treated with symptomatic treatment or kidney transplantation. In this study, the ESRD rate was higher in patients with hematuria than in those without hematuria (17.02% vs. 8.40%). In addition, Cox proportional-hazards regression and Kaplan-Meier survival analyses both demonstrated that hematuria was an independent factor associated with ESRD in SRNS patients. This result was also in line with Zagury *et al.*'s study.<sup>34</sup> Nevertheless, there are also conflicting findings showing that hematuria is not an independent factor associated with ESRD.<sup>9,37</sup> Therefore, the prognostic value of hematuria requires to be further investigated.

Several limitations to this study should be pointed out. This was a single-center, retrospective study with relatively small sample size. In addition, our study found that female SRNS patients had a higher risk of developing ESRD than male, which has not been reported in previous studies. In the future, a well-designed multi-center, large prospective study should be conducted to verify the findings of this study.

## CONCLUSION

Our results showed that 68.07% of SRNS patients could achieve CR or PR, and 10.84% of cases developed ESRD during the median follow-up duration of 4.64 years. Female, hematuria and PSR type were significantly associated with ESRD in patients with SRNS.

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