

## **SUPPLEMENTARY MATERIAL**

**Full title:**

**Characteristics of Acute Ischemic Stroke in Patients with Nephrotic Syndrome**

**Supplementary Figure 1.** Flow of study selection. NS indicates nephrotic syndrome; IS, ischemic stroke.

**Supplementary Table 1.** The results of kidney biopsy and etiology of nephrotic syndrome.

**Supplementary Table 2.** The stages of chronic kidney disease in patients with nephrotic syndrome.

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**Supplementary Table 8.** Demographic features and clinical courses of ischemic stroke patients, with and without nephrotic syndrome.

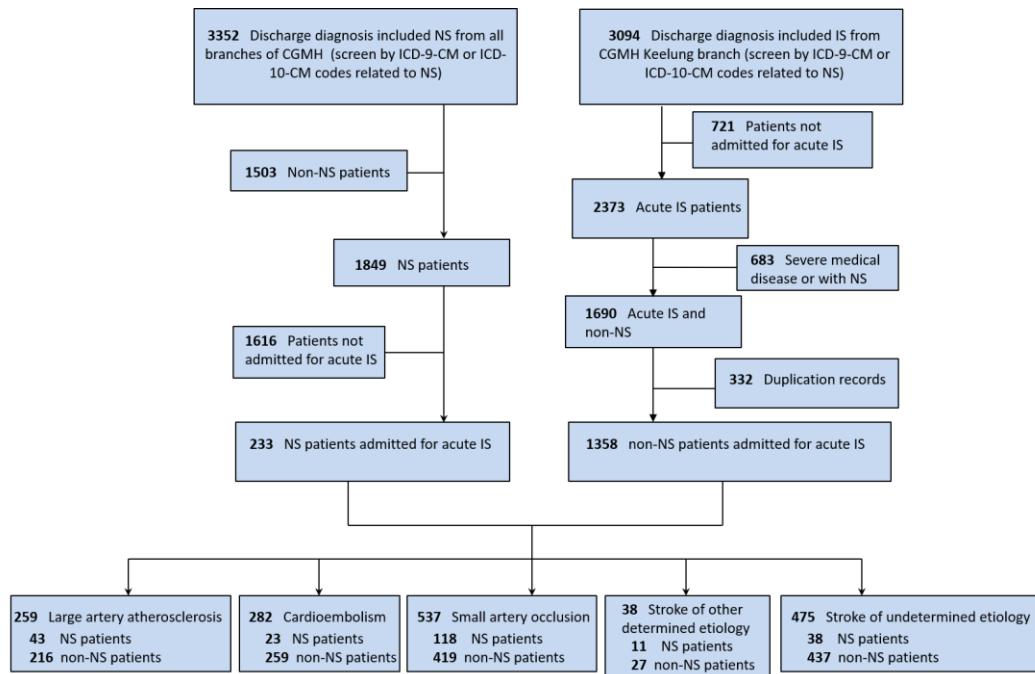
**Supplementary Table 9.** Laboratory findings of ischemic stroke patients, with and without nephrotic syndrome.

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**Supplementary Table 12.** Treatment, complication and clinical outcomes of ischemic stroke patients, with and without nephrotic syndrome.

**Supplementary Figure 1.** Flow of study selection. NS indicates nephrotic syndrome; IS, ischemic stroke.



**Supplementary Table 1.** The results of kidney biopsy and etiology of nephrotic syndrome.

	Total nephrotic syndrome patients (n=233)
With kidney biopsy (n=34)	
Membranous glomerulonephritis	16 (6.9%)
Minimal change nephropathy	1 (0.4%)
Focal segmental glomerulosclerosis	1 (0.4%)
Diffuse mesangial	1 (0.4%)
proliferative glomerulonephritis	
IgM nephropathy	1 (0.4%)
IgA nephropathy	2 (0.9%)
Amyloidosis	3 (1.3%)
Systemic lupus erythematosus	6 (2.6%)
Diabetic nephropathy (biopsy confirmed)	3 (1.3%)
Without kidney biopsy (n=199)	
Diabetic nephropathy	118 (50.6%)
Unknown	81 (34.8%)

**Supplementary Table 2.** The stages of chronic kidney disease in patients with nephrotic syndrome.

	Nephrotic syndrome N=233
Chronic kidney disease stage 1	29 (12.4%)
Chronic kidney disease stage 2	51 (21.9%)
Chronic kidney disease stage 3	74 (31.8%)
Chronic kidney disease stage 4	36 (15.5%)
Chronic kidney disease stage 5 (without hemodialysis or peritoneal dialysis)	29 (12.4%)
Chronic kidney disease stage 5 (with hemodialysis or peritoneal dialysis)	14 (6.0%)

**Supplementary Table 3.** Demographic features of ischemic stroke patients with and without nephrotic syndrome.

	Nephrotic syndrome (n=233)	No nephrotic syndrome (n=1358)	Odds ratio (95% CI)	P value
Age (year-old)	60.58±13.35	69.64±13.28		<0.001*
Male	145 (62.2%)	837 (61.6%)	1.03 (0.77-1.37)	0.462
Height (cm)	162.58±7.62	160.47±9.61		0.092
Body weight (kg)	62.92±10.68	64.35±14.48		0.218
BMI (kg/m <sup>2</sup> )	26.06±5.12	25.10±6.11		0.291
SBP at admission (mmHg)	169.95±27.15	159.06±29.79		0.032*
DBP at admission (mmHg)	90.74±17.76	87.35±18.25		0.302
Risk factors				
Hypertension	195 (83.7%)	1014 (74.7%)	1.74 (1.20-2.52)	0.001†
Diabetes mellitus	152 (65.2%)	574 (42.3%)	2.56 (1.92-3.43)	<0.001†
Hyperlipidemia	149 (63.9%)	759 (55.9%)	1.40 (1.05-1.87)	0.013†
Coronary artery disease	35 (15.0%)	146 (10.8%)	1.47 (0.99-2.19)	0.040†
Congestive heart failure	32 (13.7%)	81 (6.0%)	2.51 (1.62-3.88)	<0.001†
Previous TIA	15 (6.4%)	45 (3.3%)	2.01 (1.10-3.66)	0.022†
Atrial fibrillation	23 (9.9%)	285 (21.0%)	0.41 (0.26-0.65)	<0.001†
Hyperuricemia	40 (17.2%)	140 (10.3%)	1.80 (1.23-2.64)	0.002†
PAOD	9 (3.9%)	17 (1.3%)	3.17 (1.40-7.20)	0.009†
Smoking	22 (9.4%)	218 (16.1%)	0.55 (0.34-0.87)	0.005†
Other diseases				
COPD	12 (5.2%)	71 (5.2%)	0.98 (0.53-1.85)	0.557
Systemic lupus erythematosus	6 (2.6%)	2 (0.1%)	17.92 (3.60-89.34)	<0.001†
Lab data				
WBC (1000/ $\mu$ L)	8209.01±3079.67	8399.18±3108.89		0.393
Hemoglobin (g/dL)	12.02±2.22	13.62±2.09		<0.001*
Platelet (1000/ $\mu$ L)	220.94K±77.51K	229.99K±77.49K		0.104
INR	1.03±0.28	1.02±0.28		0.470
APTT/NC	1.02±0.98	0.98±0.98		0.260
Fibrinogen (mg/dL)	441.54±172.69	334.89±123.19		<0.001*
Sugar (mg/dL)	169.16±95.49	143.81±70.97		0.014*
Glycohemoglobin (%)	8.05±2.44	6.77±1.86		<0.001*
Hs-CRP (mg/L)	13.45±11.96	15.23±10.54		0.588
ESR (mm/hr)	44.84±32.87	16.68±17.12		<0.001*

BUN (mg/dL)	31.06±11.80	16.19±6.08	<0.001*
Creatinine (mg/dL)	2.85±1.24	0.92±0.61	<0.001*
eGFR (mL/min/1.73 m <sup>2</sup> )	46.57±29.81	79.84±14.82	<0.001*
AST (U/L)	26.63±18.33	31.45±11.21	0.117
ALT (U/L)	23.18±19.44	25.92±15.23	0.164
Total cholesterol (mg/dL)	234.38±88.97	183.36±42.86	<0.001*
Triglyceride (mg/dL)	208.24±96.21	134.78±41.15	<0.001*
LDL (mg/dL)	154.57±45.60	117.41±38.65	<0.001*
HDL (mg/dL)	40.79±16.07	41.22±13.50	0.709
Uric acid (mg/dL)	6.60±1.94	5.48±2.22	<0.001*
Sodium (mmol/L)	138.67±4.38	138.77±3.78	0.734
Potassium (mmol/L)	4.04±0.78	4.07±0.91	0.900
Calcium (mg/dL)	8.38±1.16	8.70±0.98	0.007*
Phosphate (mg/dL)	4.03±1.51	4.02±2.42	0.649
Albumin (g/dL)	2.82±0.77	3.58±0.56	<0.001*
Total protein (g/dL)	5.69±2.01	5.75±1.21	0.550

CI = confidence interval; BMI= body mass index; SBP = systolic blood pressure; DBP

= diastolic blood pressure; TIA = transient ischemic attack; PAOD = peripheral arterial

occlusive disease; COPD = chronic obstructive lung disease; WBC = white blood cells;

INR = international normalized ratio; APTT/NC = activated partial thromboplastin

time/normal control; hs-CRP = high-sensitivity C-reactive protein; ESR = erythrocyte

sedimentation rate; BUN = blood urea nitrogen; eGFR = estimated glomerular filtration

rate; AST = aspartate transaminase; ALT = alanine aminotransferase; LDL = low-

density lipoprotein; HDL= high-density lipoprotein.

Data are presented as mean ± standard deviation or n (%).

\*P < 0.05, Student t test; † P < 0.05, Chi-square test

**Supplementary Table 4.** Logistic regression for predictors of dependent functional status (modified Rankin Scale score  $\geq 3$ ) in patients with ischemic stroke following the 30-day period.

Variables	Univariate Logistic Regression		Multivariate Logistic Regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.03 (1.02-1.03)	<0.001*	1.02 (1.01-1.03)	0.002†
Male	0.70 (0.57-0.86)	0.001*	0.76 (0.60-0.98)	0.035†
Hypertension	1.01 (0.81-1.28)	0.914		
Diabetes mellitus	1.02 (0.84-1.24)	0.836		
Hyperlipidemia	0.71 (0.58-0.87)	0.001*		
CAD	1.19 (0.87-1.63)	0.269		
CHF	2.74 (1.80-4.18)	<0.001*		
Atrial fibrillation	2.95 (2.25-3.85)	<0.001*	1.44 (1.02-2.04)	0.040†
Nephrotic syndrome	2.07 (1.55-2.76)	<0.001*	4.02 (2.39-6.76)	<0.001†
Hyperuricemia	0.83 (0.61-1.13)	0.236		
TACS	28.55 (15.01-54.34)	<0.001*	13.72 (6.96-27.04)	<0.001†
Pneumonia	13.50 (9.00-20.55)	<0.001*	5.69 (3.64-8.89)	<0.001†
Pulmonary edema	39.21 (5.37-286.48)	<0.001*	9.58 (1.20-76.26)	0.033†
WBC count $> 10000$ $1000/\mu\text{L}$	2.07 (1.61-2.67)	<0.001*	1.52 (1.11-2.08)	0.008†
Hemoglobin $< 12$ g/dL	2.40 (1.87-3.08)	<0.001*	1.52 (1.10-2.08)	0.010†
eGFR $< 60$ mL/min/ $1.73\text{ m}^2$	1.87 (1.32-2.65)	<0.001*	0.54 (0.29-1.02)	0.056
Sodium $< 135$ mmol/L	2.12 (1.49-3.02)	<0.001*		
hs-CRP $> 3$ mg/L	3.85 (3.05-4.85)	<0.001*	2.20 (1.67-2.89)	<0.001†

OR = odds ratio; CI = confidence interval; CAD = coronary artery disease; CHF = congestive heart failure; TACS = total anterior circulation syndrome; eGFR = estimated glomerular filtration rate; WBC = white blood cell; hs-CRP = high-sensitivity C-reactive protein.

\* $P < 0.1$  for the univariate logistic regression, and † $P < 0.05$  for the stepwise multivariate logistic regression.

**Supplementary Table 5.** Clinical courses of ischemic stroke patients with and without nephrotic syndrome.

	Nephrotic syndrome (n=233)	No nephrotic syndrome (n=1358)	Odds ratio (95% CI)	P value
<b>Clinical syndromes</b>				
TACS	15 (6.4%)	205 (15.1%)	0.39 (0.23-0.67)	<0.001†
PACS	67 (28.8%)	421 (31.0%)	0.90 (0.66-1.22)	0.272
LACS	90 (38.6%)	517 (38.1%)	1.02 (0.77-1.36)	0.463
POCS	60 (25.8%)	218 (16.1%)	1.82 (1.31-2.52)	<0.001†
<b>TOAST classification</b>				
Large-artery atherosclerosis	43 (18.45%)	216 (15.91%)	1.20 (0.84-1.73)	0.316
Cardioembolism	23 (9.87%)	259 (19.07%)	0.47 (0.30-0.73)	<0.001†
Small-artery occlusion	118 (50.64%)	419 (30.85%)	2.32 (1.75-3.08)	<0.001†
Stroke of other determined etiology	11 (4.72%)	27 (1.99%)	2.44 (1.20-5.00)	0.012†
Stroke of undetermined etiology	38 (16.31%)	437 (32.18%)	0.43 (0.30-0.61)	<0.001†
Intra-arterial thrombectomy	0 (0%)	2 (0.1%)		0.728
Intra-venous thrombolysis	4 (1.7%)	74 (5.4%)	0.30 (0.11-0.84)	0.006†
Mean length of stay in the acute medicine ward (days)	14.73±12.35	13.42±10.19		0.086
Stroke in evolution	29 (12.4%)	181 (13.3%)	0.92 (0.61-1.41)	0.403
<b>Complication at admission</b>				
Pneumonia	40 (17.2%)	248 (18.3%)	0.93 (0.64-1.34)	0.384
GI bleeding	21 (9.0%)	134 (9.9%)	0.91 (0.56-1.47)	0.395
Urinary tract infection	29 (12.4%)	184 (13.5%)	0.91 (0.60-1.38)	0.368
Other infection	17 (7.3%)	67 (4.9%)	1.52 (0.87-1.63)	0.095
Acute coronary syndrome	3 (1.3%)	19 (1.4%)	0.92 (0.27-3.13)	0.594
Venous thromboembolism	2 (0.9%)	5 (0.4%)	2.34 (0.45-12.15)	0.273
Pulmonary edema	13 (5.6%)	25 (1.8%)	3.15 (1.59-6.25)	0.002†
<b>Medication during admission</b>				
Warfarin	13 (5.6%)	47 (3.5%)	1.65 (0.88-3.10)	0.088
Aspirin	143 (61.4%)	853 (62.8%)	0.96 (0.72-1.27)	0.402
P2Y12 inhibitors	57 (24.5%)	264 (19.4%)	1.34 (0.97-1.86)	0.049†
Heparin in acute stage	10 (4.3%)	25 (1.8%)	2.39 (1.13-5.05)	0.024†
NOACs	1 (0.4%)	146 (10.8%)	0.04 (0.01-0.26)	<0.001†
Statins	82 (35.2%)	596 (43.9%)	0.69 (0.52-0.93)	0.008†
<b>Glasgow coma scale score</b>				
Upon admission	15 (15-15)	15 (15-15)		0.001*

Upon discharge	15 (15-15)	15 (15-15)	<0.001*
NIHSS score			
Upon admission	6 (4-14)	4 (3-9)	0.087
Upon discharge	6 (3-18)	4 (3-10)	0.241
modified Rankin scale score			
Upon admission	3 (2-4)	2 (1-4)	<0.001*
Upon admission	3 (2-4)	2 (1-4)	<0.001*
Death within 30 days	8 (3.4%)	64 (4.7%)	0.72 (0.34-1.52)
Recurrent stroke within 30 days	0 (0%)	7 (0.5%)	0.331
modified Rankin scale score $\geq 3$	151 (64.8%)	640 (47.1%)	2.07 (1.55-2.76)

CI = confidence interval; TACS = total anterior circulation syndrome; PACS = partial

anterior circulation syndrome; LACS = lacunar syndrome; POCS = posterior

circulation syndrome; TOAST = Trial of ORG 10172 in Acute Stroke Treatment; GI =

gastrointestinal; NOACs = non-vitamin K antagonist oral anticoagulants; NIHSS =

national institute of health stroke scale.

Data are presented as mean  $\pm$  standard deviation, median (interquartile range) or n (%).

\*P < 0.05, Student t test or Mann-Whitney U test; † P < 0.05, Chi-square test

**Supplementary Table 6.** Primary and secondary endpoints of ischemic stroke patients with and without nephrotic syndrome, specified in Keelung branch of Chang Gung Memorial Hospital, from 2016 to 2017.

	Nephrotic syndrome (n=17)	No nephrotic syndrome (n=769)	P value
Death within 30 days	1 (5.9%)	38 (4.9%)	0.217
Recurrent stroke within 30 days	0 (0%)	4 (0.5%)	0.911
modified Rankin scale score $\geq 3$	13 (76.5%)	320 (41.6%)	
Odds ratio (95% CI)	4.56 (1.47-14.11)	1	0.004†
Adjusted odds ratio (95% CI)	3.95 (1.10-14.11)	1	0.035‡

CI = confidence interval.

Data are presented as n (%).

† $P < 0.05$ , Chi-square test; ‡  $P < 0.05$ , adjusted odds ratio and P value using multivariate logistic regression analysis, variates include age, male gender, hyperlipidemia, congestive heart failure, atrial fibrillation, nephrotic syndrome, total anterior circulation syndrome, pneumonia, pulmonary edema, white blood cell count  $> 10000$   $1000/\mu\text{L}$ , Hemoglobin  $< 12$  g/dL, estimated glomerular filtration rate  $< 60$  mL/min/ $1.73 \text{ m}^2$ , Sodium  $< 135$  mmol/L, and high-sensitivity C-reactive protein  $> 3$  mg/L.

**Supplementary Table 7.** Primary and secondary endpoints of ischemic stroke

patients with and without nephrotic syndrome, specified in the group with estimated glomerular filtration rate  $\geq 60$  mL/min/1.73 m<sup>2</sup>.

	Nephrotic syndrome (n=80)	No nephrotic syndrome (n=1358)	P value
Death within 30 days	1 (1.2%)	64 (4.7%)	0.111
Recurrent stroke within 30 days	0 (0%)	7 (0.5%)	0.669
modified Rankin scale score $\geq 3$	53 (66.2%)	640 (47.1%)	
Odds ratio (95% CI)	2.20 (1.37-3.54)	1	0.001†
Adjusted odds ratio (95% CI)	4.24 (2.51-7.14)	1	<0.001‡

CI = confidence interval.

Data are presented as n (%).

†P < 0.05, Chi-square test; ‡ P < 0.05, adjusted odds ratio and P value using multivariate logistic regression analysis, variates include age, male gender, hyperlipidemia, congestive heart failure, atrial fibrillation, nephrotic syndrome, total anterior circulation syndrome, pneumonia, pulmonary edema, white blood cell count > 10000 1000/ $\mu$ L, Hemoglobin < 12 g/dL, Sodium < 135 mmol/L, and high-sensitivity C-reactive protein > 3 mg/L.

**Supplementary Table 8.** Demographic features and clinical courses of ischemic stroke patients, with and without nephrotic syndrome.

	Large-artery atherosclerosis		Cardioembolism		Small-artery occlusion		Stroke of other determined etiology		Stroke of undetermined etiology	
	NS (n=43)	No NS (n=216)	NS (n=23)	No NS (n=259)	NS (n=118)	No NS (n=419)	NS (n=11)	No NS (n=27)	NS (n=38)	No NS (n=437)
Age (years)	60.16±15.39	68.59±12.53	68.35±10.42	76.47±11.49	61.03±10.20	67.08±12.47	36.91±14.69	53.93±14.86	61.77±13.71	69.48±13.50
P value	<0.001*		0.001*		<0.001*		0.003*		0.001*	
Male (%)	25 (58.1%)	142 (65.7%)	16 (69.6%)	135 (52.1%)	75 (63.6%)	266 (63.5%)	6 (54.5%)	13 (48.1%)	24 (63.2%)	277 (63.4%)
OR (95% CI)	0.71 (0.37-1.39)		2.08 (0.83-5.23)		0.98 (0.64-1.50)		1.29 (0.32-5.28)		0.91 (0.47-1.79)	
P value	0.206		0.084		0.511		0.500		0.458	
Height (cm)	161.67±8.13	161.24±9.05	164.55±3.02	158.19±5.78	162.02±7.97	160.51±9.56	165.83±10.01	160.61±8.99	163.50±6.59	161.41±7.51
P value	0.875		0.206		0.498		0.236		0.538	
Weight (kg)	61.40±15.41	65.32±14.54	67.26±4.16	60.26±13.21	64.36±9.35	67.46±10.20	57.33±4.23	58.28±10.18	58.36±10.80	63.30±13.95
P value	0.256		<0.001*		0.049*		0.759		0.209	
BMI (kg/m <sup>2</sup> )	25.64±4.70	25.28±5.32	24.67±1.58	24.99±3.44	27.34±9.48	25.86±4.55	19.54±1.18	22.52±3.94	23.76±2.31	24.48±3.38
P value	0.836		0.940		0.222		0.218		0.435	
SBP at admission (mmHg)	175.17±29.47	162.69±31.21	160.33±37.29	153.40±31.14	176.20±27.64	164.68±26.38	160±28.10	152.83±30.76	156.89±20.94	155.57±30.29
P value	0.373		0.712		0.089		0.838		0.899	
DBP at admission (mmHg)	95.80±29.04	87.08±18.22	88.50±23.53	88.60±22.43	91.72±18.68	88.04±15.94	90.01±22.88	95.67±17.11	86.56±10.62	85.37±17.85
P value	0.352		0.995		0.400		0.771		0.846	
Risk factors (%)										
Hypertension	38 (88.4%)	171 (79.2%)	21 (91.3%)	185 (71.4%)	101 (85.6%)	341 (81.4%)	7 (63.6%)	9 (33.3%)	29 (76.3%)	302 (69.1%)
OR (95% CI)	1.96 (0.73-5.26)		4.14 (0.95-18.12)		1.31 (0.74-2.31)		3.50 (0.81-15.16)		1.28 (0.61-2.70)	

P value	0.126	0.029†	0.219	0.088	0.329
DM	30 (69.8%)	124 (57.4%)	7 (30.4%)	81 (31.3%)	95 (80.5%)
OR (95% CI)	1.69 (0.84-3.43)		0.96 (0.38-2.41)		4.82 (2.94-7.90)
P value	0.095	0.565		<0.001†	0.179
Hyperlipidemia	30 (69.8%)	143 (66.2%)	7 (30.4%)	93 (35.9%)	82 (69.5%)
OR (95% CI)	1.16 (0.57-2.36)		0.78 (0.31-1.96)		1.30 (0.84-2.01)
P value	0.412	0.385		0.146	0.198
CAD	3 (7.0%)	23 (10.6%)	6 (26.1%)	41 (15.8%)	19 (16.1%)
OR (95% CI)	0.43 (0.13-1.47)		1.87 (0.70-5.02)		2.03 (1.11-3.69)
P value	0.124	0.166		0.018†	0.711
CHF	8 (18.6%)	5 (2.3%)	6 (26.1%)	47 (18.1%)	12 (10.2%)
OR (95% CI)	9.60 (2.97-31.03)		1.58 (0.59-4.23)		5.12 (2.10-12.47)
P value	<0.001†	0.250		<0.001†	0.501
AF	0 (0%)	4 (1.9%)	20 (87.0%)	245 (94.6%)	2 (1.7%)
OR (95% CI)			0.35 (0.09-1.35)		0.70 (0.15-3.24)
P value	0.480	0.133		0.484	
Hyperuricemia	10 (23.3%)	18 (8.3%)	8 (34.8%)	29 (11.2%)	14 (11.9%)
OR (95% CI)	3.31 (1.41-7.81)		4.21 (1.64-10.79)		1.09 (0.57-2.05)
P value	0.008†	0.005†		0.459	0.134
PAOD	3 (7.0%)	4 (1.9%)	1 (4.3%)	7 (2.7%)	4 (3.4%)
OR (95% CI)	3.96 (0.85-18.36)		1.63 (0.19-13.86)		14.56 (1.61-131.56)
P value	0.093	0.500		0.009†	0.711
Smoking	4 (9.3%)	34 (15.7%)	0 (0%)	28 (10.8%)	15 (12.7%)
OR (95% CI)	0.55 (0.18-1.63)			0.76 (0.42-1.38)	
P value	0.197	0.080		0.227	0.347
Previous TIA	2 (4.7%)	8 (3.7%)	2 (8.7%)	9 (3.5%)	9 (7.6%)
OR (95% CI)	1.26 (0.26-6.16)		2.64 (0.53-12.99)		3.35 (1.33-8.45)
					2.60 (0.15-45.68)
					0.65 (0.08-5.00)

<i>P</i> value	0.519	0.224	0.012†	0.501	0.555
Other diseases					
COPD	5 (11.6%)	11 (5.1%)	4 (17.4%)	15 (5.8%)	2 (1.7%)
OR (95% CI)	2.44 (0.80-7.42)		3.41 (1.03-11.30)		0.34 (0.08-1.48)
<i>P</i> value	0.107		0.058		0.101
SLE	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
OR (95% CI)					15.00 (2.32-96.96)
<i>P</i> value					0.004†
Clinical syndromes					
TACS	8 (18.6%)	50 (23.1%)	6 (26.1%)	111 (42.9%)	0 (0%)
OR (95% CI)	0.75 (0.33-1.73)		0.47 (0.18-1.22)		
<i>P</i> value	0.328		0.085		0.238
PACS	13 (30.2%)	78 (36.1%)	7 (30.4%)	96 (37.1%)	19 (16.1%)
OR (95% CI)	0.76 (0.38-1.55)		0.74 (0.29-1.86)		15.78 (5.75-43.28)
<i>P</i> value	0.283		0.343		<0.001†
LACS	8 (18.6%)	24 (11.1%)	4 (17.4%)	21 (8.1%)	72 (61.0%)
OR (95% CI)	1.82 (0.76-4.38)		2.38 (0.74-7.63)		0.19 (0.11-0.30)
<i>P</i> value	0.137		0.134		<0.001†
POCS	14 (32.6%)	63 (29.2%)	6 (26.1%)	30 (11.6%)	27 (22.9%)
OR (95% CI)	1.17 (0.58-2.35)		2.68 (0.98-7.33)		2.87 (1.67-4.93)
<i>P</i> value	0.398		0.057		<0.001†
					0.347
					0.522
					0.174

NS = nephrotic syndrome; OR = odds ratio; CI = confidence interval; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure;

DM = diabetes mellitus; CAD = coronary artery disease; CHF = congestive heart failure; AF = atrial fibrillation; PAOD = peripheral arterial occlusive disease;

TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease; SLE = Systemic lupus erythematosus; TACS = total anterior circulation syndrome; PACS = partial anterior circulation syndrome; LACS = lacunar syndrome; POCS = posterior circulation syndrome;. Data are presented as mean  $\pm$  standard deviation or n (%).

\* $P < 0.05$ , Student t test; † $P < 0.05$ , Chi-square test

**Supplementary Table 9.** Laboratory findings of ischemic stroke patients, with and without nephrotic syndrome.

	Large-artery atherosclerosis		Cardioembolism		Small-artery occlusion		Stroke of other determined etiology		Stroke of undetermined etiology	
	NS (n=43)	No NS (n=216)	NS (n=23)	No NS (n=259)	NS (n=118)	No NS (n=419)	NS (n=11)	No NS (n=27)	NS (n=38)	No NS (n=437)
WBC (1000/ $\mu$ L)	8316.28±2729	9250.79±3816	7952.17±2169	8326.72±3133	7855.56±3176	7766.81±2277	8845.45±4488	10561.90±617	9123.08±3070	8498.76±2989
	.11	.00	.39	.81	.65	.36	.29	4.50	.78	.05
P value	0.130		0.576		0.783		0.422		0.217	
Hemoglobin (g/dL)	11.89±2.41	13.85±2.23	12.64±2.31	13.29±2.04	11.99±2.06	13.94±1.81	12.33±3.92	12.04±3.16	11.77±1.84	13.49±2.15
P value	<0.001*		0.148		<0.001*		0.820		<0.001*	
Platelet (1000/ $\mu$ L)	205.63K±76.2	232.59±67.87	231.35K±72.6	214.27K±78.6	217.36K±72.8	228.39K±67.9	212.55K±112.	244.36K±103.	244.77K±80.0	239.41K±86.4
	4K	K	3K	2K	1K	1K	42K	58K	7K	8K
P value	0.023*		0.319		0.136		0.432		0.711	
INR	0.95±0.12	0.99±0.11	1.24±0.36	1.05±0.10	1.05±0.32	0.99±0.08	1.01±0.14	1.22±0.29	0.95±0.06	1.02±0.23
P value	0.058		0.068		0.138		0.331		0.486	
APTT/NC	1.00±0.13	0.90±0.12	1.01±0.13	0.99±0.12	1.10±0.29	0.99±0.11	1.12±0.19	1.02±0.10	0.99±0.16	0.98±0.15
P value	0.518		0.331		0.334		0.069		0.737	
Glycohemoglobin (%)	8.56±2.79	7.23±2.10	6.79±1.52	6.22±0.98	8.31±2.43	6.97±2.09	6.26±1.59	6.74±2.08	7.60±2.27	6.64±1.76
P value	0.021*		0.185		<0.001*		0.645		0.063	
ESR (mm/hr)	57.44±42.59	17.51±6.54	29.20±15.07	16.53±10.68	43.80±21.32	12.90±6.13	32.75±24.72	33.45±27.08	47.67±24.16	18.99±15.3
									3	
P value	0.023*		0.152		<0.001*		0.970		0.015*	
BUN (mg/dL)	31.79±20.21	15.71±5.76	26.20±10.42	17.91±6.28	32.32±15.76	15.52±3.05	27.68±12.74	15.32±4.81	30.78±19.76	16.11±6.91
P value	<0.001*		0.001*		<0.001*		0.020*		<0.001*	

Creatinine (mg/dL)	2.79±1.82	0.93±0.28	1.82±1.01	1.13±0.99	3.07±2.02	0.94±0.23	1.92±0.85	0.87±0.25	3.17±2.11	0.97± 0.31
P value	<0.001*		0.061		<0.001*		0.007*		<0.001*	
eGFR (mL/min/1.73 m <sup>2</sup> )	46.23±30.92	81.41±14.13	53.96±25.02	76.72±14.44	45.04±30.02*	80.95±14.67	51.69±29.78	83.82±16.04	45.70±31.21	75.79±15.1 9
P value	<0.001*		<0.001*		<0.001*		0.005*		<0.001*	
Total cholesterol (mg/dL)	244.76±93.77	187.46±41.82	202.10±65.64	173.12±44.23	240.50±90.30	184.10±40.50	226.4±72.51	208.24±69.12	224.09±54.44	185.22±41. 45
P value	0.001*		0.151		<0.001*		0.531		0.012*	
Triglyceride (mg/dL)	271.62±79.43	139.70±52.61	122.70±52.76	102.86±34.92	213.41±104.5	152.12±89.28	224.40±117.1	211.67±123.5	169.84±71.17	129.77±45. 12
P value	0.002*		0.149		<0.001*		0.865		0.060	
LDL (mg/dL)	150.10±53.24	121.59±36.23	123.13±38.71	107.74±34.67	163.64±44.97	116.29±35.81	130.29±31.12	134.48±46.64	154.40±46.23	121.11±39. 81
P value	0.054		0.111		0.001*		0.865		0.018*	
HDL (mg/dL)	41.18±15.53	39.14±10.29	34.69±7.65	46.03±10.46	38.95±11.23	41.11±14.12	46.71±10.12	34.77±8.65	48.43±19.43	40.20±13.0 4
P value	0.597		<0.001*		0.158		0.122		0.070	
Uric acid (mg/dL)	6.66±1.85	5.58±1.72	6.93±2.08	5.51±1.53	6.46±1.85	5.51±1.14	7.98±2.37	5.82±1.87	6.56±2.13	5.36±1.51
P value	0.132		0.003*		<0.001*		0.047*		<0.001*	
Potassium (mmol/L)	4.06±0.78	3.91±1.13	3.71±0.90	4.05±1.10	4.01±0.61	4.43±0.78	4.60±0.70	3.87±0.47	4.17±0.75	3.82±0.45
P value	0.439		0.464		0.547		0.002*		0.011*	
Calcium (mg/dL)	8.24±0.90	8.85±0.71	8.59±1.10	8.34±1.23	8.38±0.95	8.65±1.01	8.16±0.67	8.33±0.47	8.44±0.73	8.87±0.58
P value	0.116		0.511		0.320		0.779		0.004*	
Albumin (g/dL)	2.76±0.49	3.61±0.55	2.69±0.56	3.39±0.61	2.85±0.78	3.81±0.43	2.86±1.02	2.18±0.38	2.88±0.72	3.60±0.62
P value	<0.001*		<0.001*		<0.001*		0.107		<0.001*	
Fibrinogen (mg/dL)	473.00±197.4	320.27±151.7	731.50±395.2	428.86±182.1	396.79±117.0	298.70±43.56	341.67±112.4	320.10±116.1	465.15±157.4	336.06±110.2

	0	6	7	5	9	8	7	8	3	
P value	0.086		0.138		0.010*		0.789		0.008*	
Sugar (mg/dL)	178.11±98.66	162.95±74.95	126.63±36.54	155.55±94.61	180.93±97.52	143.59±46.82	95.40±7.80	251.50±117.4	169.82±88.45	123.03±49.19
P value	0.593		0.132		0.014*		0.431		0.050	
Hs-CRP (mg/L)	21.91±19.68	18.29±13.52	14.41±13.32	24.06±22.12	10.18±9.23	7.04±6.53	5.61±8.96	42.15±33.79	14.94±13.68	12.69±10.77
P value	0.654		0.473		0.321		0.225		0.675	
AST (U/L)	26.39±14.42	32.71±23.17	35.68±22.24	30.84±15.41	26.31±19.48	29.95±24.65	23.29±13.95	34.50±25.03	22.68±11.80	32.26±17.33
P value	0.152		0.405		0.505		0.313		0.302	
ALT (U/L)	27.03±12.38	26.82±17.52	21.74±19.97	25.35±10.87	23.10±15.81	24.97±17.22	18.00±7.11	32.79±20.27	21.00±10.24	26.40±12.72
P value	0.966		0.405		0.384		0.010*		0.404	
Sodium (mmol/L)	138.26±5.74	138.61±3.82	139.54±3.79	138.91±4.28	139.06±4.20	138.92±3.61	137.91±3.53	138.47±7.00	137.61±3.67	138.61±3.36
P value	0.633		0.510		0.764		0.808		0.093	
Phosphate (mg/dL)	3.78±1.57	3.28±0.69	3.35±1.39	3.70±0.97	3.15±1.59	5.67±2.05	4.13±1.02	4.85±1.91	4.36±1.29	3.98±1.94
P value	0.496		0.567		0.600		0.497		0.496	
Total protein (g/dL)	5.32±0.91	6.48±0.64	5.48±1.15	5.62±1.26	5.40±1.01	5.16±1.80	5.60±1.10	4.90±0.28	5.68±0.93	5.47±1.15
P value	0.003*		0.775		0.546		0.463		0.346	

NS = nephrotic syndrome; WBC = white blood cells; INR = international normalized ratio; APTT/NC = activated partial thromboplastin time/normal control;

ESR = erythrocyte sedimentation rate; BUN = blood urea nitrogen; eGFR = estimated glomerular filtration rate; LDL = low-density lipoprotein; HDL= high-density lipoprotein; hs-CRP = high-sensitivity C-reactive protein; AST = aspartate transaminase; ALT = alanine aminotransferase.

Data are presented as mean ± standard deviation.

\* $P < 0.05$ , Student t test



**Supplementary Table 10.** Logistic regression for predictors of dependent functional status (modified Rankin Scale score  $\geq 3$ ) in patients with small-artery occlusion following the 30-day period.

Variables	Univariate Logistic Regression		Multivariate Logistic Regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.01 (0.99-1.03)	0.465		
Male	0.90 (0.60-1.35)	0.607		
Hypertension	1.47 (0.84-2.56)	0.177		
Diabetes mellitus	1.45 (0.97-2.15)	0.069*		
Hyperlipidemia	0.88 (0.59-1.32)	0.532		
CAD	0.72 (0.36-1.44)	0.355		
CHF	1.89 (1.76-4.65)	0.169		
Atrial fibrillation	0.99 (0.27-3.72)	0.991		
Nephrotic syndrome	6.98 (4.45-10.95)	<0.001*	8.02 (3.94-16.32)	<0.001†
Hyperuricemia	0.82 (0.43-1.58)	0.560		
Pneumonia	3.19 (1.44-7.07)	0.004*		
WBC count > 10000 1000/ $\mu$ L	1.19 (0.69-2.05)	0.538		
Hemoglobin < 12 g/dL	3.53 (2.25-5.54)	<0.001*		
eGFR<60 mL/min/1.73 $m^2$	5.07 (3.06-8.41)	<0.001*	0.66 (0.29-1.53)	0.333
Sodium < 135 mmol/L	1.67 (0.85-3.31)	0.139		
hs-CRP > 3 mg/L	1.92 (1.18-3.13)	0.009*	1.85 (1.06-3.21)	0.030†

OR = odds ratio; CI = confidence interval; CAD = coronary artery disease; CHF =

congestive heart failure; WBC = white blood cell; eGFR = estimated glomerular

filtration rate; hs-CRP = high-sensitivity C-reactive protein.

\* $P < 0.1$  for the univariate logistic regression, and † $P < 0.05$  for the stepwise multivariate logistic regression.

**Supplementary Table 11.** Logistic regression for predictors of dependent functional status (modified Rankin Scale score  $\geq 3$ ) in patients with stroke of undetermined etiology following the 30-day period.

Variables	Univariate Logistic Regression		Multivariate Logistic Regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.01 (1.00-1.03)	0.096*		
Male	0.72 (0.49-1.06)	0.093*		
Hypertension	0.89 (0.60-1.32)	0.552		
Diabetes mellitus	1.06 (0.73-1.54)	0.748		
Hyperlipidemia	0.69 (0.48-1.00)	0.052*		
CAD	1.60 (0.82-3.12)	0.165		
CHF	3.93 (1.32-11.68)	0.014*		
Atrial fibrillation	2.21 (0.92-5.33)	0.077*		
Nephrotic syndrome	2.66 (1.23-5.73)	0.013*	2.47 (1.06-5.76)	0.037†
Hyperuricemia	0.75 (0.42-1.34)	0.329		
TACS	31.65 (4.30-232.72)	0.001*	17.55 (2.30-133.96)	0.006†
Pneumonia	7.87 (3.83-16.16)	<0.001*	4.12 (1.89-9.00)	<0.001†
WBC count > 10000 1000/ $\mu$ L	2.03 (1.25-3.30)	0.004*		
Hemoglobin < 12 g/dL	2.10 (1.31-3.37)	0.002*		
eGFR<60 mL/min/1.73 $m^2$	1.97 (0.81-4.82)	0.135		
Sodium < 135 mmol/L	2.47 (1.22-5.00)	0.012*		
hs-CRP > 3 mg/L	3.30 (2.16-5.04)	<0.001*	2.19 (1.36-3.50)	0.001†

OR = odds ratio; CI = confidence interval; CAD = coronary artery disease; CHF = congestive heart failure; TACS = total anterior circulation syndrome; WBC = white blood cell; eGFR = estimated glomerular filtration rate; hs-CRP = high-sensitivity C-reactive protein.

\* $P < 0.1$  for the univariate logistic regression, and † $P < 0.05$  for the stepwise multivariate logistic regression.

**Supplementary Table 12.** Treatment, complication and clinical outcomes of ischemic stroke patients, with and without nephrotic syndrome.

Large-artery atherosclerosis		Cardioembolism		Small-artery occlusion		Stroke of other determined etiology		Stroke of undetermined etiology	
NS (n=43)	No NS (n=216)	NS (n=23)	No NS (n=259)	NS (n=118)	No NS (n=419)	NS (n=11)	No NS (n=27)	NS (n=38)	No NS (n=437)
<b>Treatment</b>									
Intra-venous thrombolysis	0 (0%)	13 (6%)	1 (4.3%)	34 (13.1%)	2 (1.7%)	11 (2.6%)	1 (9.1%)	0 (0%)	0 (0%)
OR (95% CI)				0.30 (0.04-2.29)		0.64 (0.14-2.90)			
P value	0.088		0.188		0.425		0.289		0.247
Intra-arterial thrombectomy	0 (0%)	1 (0.5%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
OR (95% CI)									
P value	0.833		0.918						
Warfarin	3 (7.0%)	12 (5.6%)	4 (17.4%)	19 (7.3%)	3 (2.5%)	2 (0.5%)	2 (18.2%)	1 (3.7%)	1 (2.6%)
OR (95% CI)	1.27 (0.34-4.70)		2.65 (0.82-8.58)		5.40 (0.89-32.70)		5.78 (0.47-71.62)		0.85 (0.11-6.71)
P value	0.471		0.105		0.074		0.196		0.677
P2Y12 inhibitors	16 (37.2%)	67 (31.0%)	6 (26.1%)	32 (12.4%)	25 (21.2%)	64 (15.3%)	1 (9.1%)	2 (7.4%)	9 (23.7%)
OR (95% CI)	1.31 (0.66-2.59)		2.49 (0.92-6.79)		1.48 (0.88-2.48)		1.25 (0.10-15.38)		1.05 (0.48-2.28)
P value	0.273		0.072		0.090		0.653		0.523
Heparin in acute stage	4 (9.3%)	12 (5.6%)	1 (4.3%)	3 (1.2%)	4 (3.4%)	1 (0.2%)	1 (9.1%)	0 (0%)	9 (2.1%)
OR (95% CI)	1.74 (0.53-5.66)		3.86 (0.39-38.72)		14.56 (1.61-131.56)				
P value	0.267		0.291		0.009†		0.289		0.459

Aspirin	25 (58.1%)	130 (60.2%)	10 (43.5%)	54 (20.8%)	82 (69.5%)	357 (85.2%)	5 (45.5%)	16 (59.3%)	23 (60.5%)	292 (66.8%)
OR (95% CI)	0.91 (0.47-1.77)		2.91 (1.21-6.99)		0.38 (0.23-0.61)		0.57 (0.14-2.36)		0.70 (0.36-1.37)	
P value	0.452		0.018†		<0.001†		0.337		0.195	
NOACs	0 (0%)	3 (1.4%)	1 (4.3%)	128 (49.4%)	0 (0%)	4 (1.0%)	0 (0%)	0 (0%)	0 (0%)	11 (2.5%)
OR (95% CI)			0.05 (0.01-0.35)							
P value	0.577		<0.001†		0.367				0.385	
Statins	17 (39.5%)	118 (54.6%)	4 (17.4%)	74 (28.6%)	44 (37.3%)	209 (49.9%)	2 (18.2%)	7 (25.9%)	15 (39.5%)	185 (42.3%)
OR (95% CI)	0.54 (0.28-1.05)		0.52 (0.17-1.59)		0.59 (0.39-0.90)		0.64 (0.11-3.68)		0.85 (0.43-1.66)	
P value	0.047†		0.181		0.008†		0.478		0.376	
Length of stay in acute care unit (days)	18.81±16.59	16.30±11.01	22.74±19.34	17.72±12.99	11.02±8.44	8.17±4.25	20.00±12.58	14.33±9.24	15.15±9.12	14.41±9.90
P value	0.215		0.258		0.001*		0.440		0.653	
Stroke in evolution	10 (23.3%)	61 (28.2%)	5 (21.7%)	56 (21.6%)	7 (5.9%)	7 (1.7%)	3 (27.3%)	6 (22.2%)	4 (10.5%)	51 (11.7%)
OR (95% CI)	0.77 (0.36-1.65)		1.00 (0.36-2.82)		3.69 (1.27-10.73)		1.31 (0.26-6.55)		0.86(0.29-2.52)	
P value	0.314		0.587		0.019†		0.522		0.518	
Complication at admission										
UTI	5 (11.6%)	32 (14.8%)	6 (26.1%)	63 (24.3%)	12 (10.2%)	23 (5.5%)	1 (9.1%)	4 (14.8%)	5 (13.2%)	62 (14.2%)
OR (95% CI)	0.75 (0.28-2.06)		1.09 (0.41-2.89)		1.93 (0.93-4.02)		0.58 (0.06-5.81)		0.89 (0.33-2.35)	
P value	0.389		0.515		0.061		0.545		0.517	
Pneumonia	12 (27.9%)	61 (28.2%)	5 (21.7%)	96 (37.1%)	11 (9.3%)	15 (3.6%)	1 (9.1%)	5 (18.5%)	11 (28.9%)	71 (16.2%)
OR (95% CI)	0.98 (0.47-2.03)		0.47 (0.17-1.30)		2.75 (1.23-6.16)		0.44 (0.05-4.27)		2.01 (0.96-4.23)	
P value	0.556		0.102		0.014†		0.429		0.054	
GI bleeding	5 (11.6%)	31 (14.4%)	2 (8.7%)	52 (20.1%)	5 (4.2%)	5 (1.2%)	1 (9.1%)	3 (11.1%)	8 (21.1%)	42 (9.6%)
OR (95% CI)	0.78 (0.29-2.14)		0.38 (0.09-1.66)		3.64 (1.04-12.78)		0.80 (0.07-8.65)		2.41 (1.04-5.59)	
P value	0.420		0.142		0.047†		0.674		0.041*	

Other infection	7 (16.3%)	11 (5.1%)	1 (4.3%)	20 (7.7%)	5 (4.2%)	12 (2.9%)	1 (9.1%)	3 (11.1%)	3 (7.9%)	20 (4.6%)
OR (95% CI)	3.61 (1.31-9.92)		0.54 (0.07-4.22)		1.49 (0.51-4.32)		0.80 (0.07-8.65)		1.73 (0.49-6.10)	
P value	0.017†		0.470		0.315		0.674		0.291	
Acute coronary syndrome	1 (2.3%)	5 (2.3%)	1 (4.3%)	7 (2.7%)	0 (0%)	1 (0.2%)	0 (0%)	2 (7.4%)	1 (2.6%)	4 (0.9%)
OR (95% CI)	1.00 (0.11-8.78)		1.63 (0.19-13.86)						2.84 (0.31-26.01)	
P value	0.738		0.500		0.779		0.499		0.350	
Venous thromboembolism	1 (2.3%)	2 (0.9%)	1 (4.3%)	2 (0.8%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
OR (95% CI)	2.54 (0.23-28.61)		5.82 (0.51-66.73)							
P value	0.423		0.227		0.779					
Pulmonary edema	4 (9.3%)	4 (1.9%)	3 (13%)	16 (6.2%)	4 (3.4%)	0 (0%)	0 (0%)	1 (3.7%)	2 (5.3%)	4 (0.9%)
OR (95% CI)	5.41 (1.30-22.55)		2.27 (0.61-8.45)						5.82 (1.03-32.86)	
P value	0.028†		0.195		0.002†		0.711		0.080	
Glasgow coma scale score										
Upon admission	15 (15-15)	15 (11-15)	15 (13-15)	14 (11-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)
P value	0.241		0.217		0.155		0.462		0.515	
Upon discharge	15 (15-15)	15 (11-15)	15 (13-15)	14 (10-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (11-15)	15 (15-15)	15 (11-15)
P value	0.255		0.100		0.906		0.222		0.207	
NIHSS score										
Upon admission	6 (3-13)	6 (3-13)	12 (10-15)	10 (4-18)	6 (3-8)	3 (2-4)	10 (6-14)	4 (3-12)	11 (3-26)	5 (3-9)
P value	0.834		0.461		0.094		0.418		0.476	
Upon discharge	6 (3-15)	6 (3-16)	12 (9-18)	9 (4-20)	4 (3-8)	3 (2-4)	14 (8-20)	5 (3-18)	12 (3-26)	5 (3-10)
P value	0.785		0.555		0.233		0.319		0.358	
mRS score										

Upon admission	4 (3-5)	3 (2-5)	3 (2-3)	5 (2-5)	3 (2-3)	1 (1-2)	2 (2-4)	2 (1-5)	3 (3-5)	3 (2-4)
P value	0.043*		0.106		<0.001*		0.868		0.112	
Upon discharge	4 (3-5)	3 (2-5)	3 (3-4)	3 (3-5)	3 (2-3)	1 (1-2)	2 (2-4)	2 (1-5)	3 (3-4)	3 (2-4)
P value	1.171		0.274		<0.001*		0.855		0.115	
Outcomes										
Death within 30 days	4 (9.3%)	18 (8.3%)	1 (4.3%)	27 (10.4%)	2 (1.7%)	1 (0.2%)	0 (0%)	6 (22.2%)	1 (2.6%)	12 (2.7%)
OR (95% CI)	1.12 (0.36-3.50)		0.39 (0.05-3.00)		7.16 (0.24-79.61)				0.93 (0.12-7.33)	
P value	0.517		0.305		0.124		0.107		0.709	
Recurrent stroke within 30 days	0 (0%)	1 (0.5%)	0 (0%)	2 (0.8%)	0 (0%)	2 (0.5%)	0 (0%)	0 (0%)	0 (0%)	2 (0.5%)
P value	0.833		0.843		0.607				0.846	
mRS score $\geq 3$	33 (76.7%)	133 (61.6%)	18 (78.3%)	182 (70.3%)	68 (57.6%)	67 (16.0%)	3 (27.3%)	12 (44.4%)	30 (78.9%)	242 (55.4%)
OR (95% CI)	2.04 (0.95-4.35)		1.50 (0.54-4.20)		7.08 (4.52-11.10)		0.47 (0.10-2.16)		2.66 (1.23-5.73)	
P value	0.043†		0.301		<0.001†		0.272		0.007†	
Adjusted OR (95% CI)	2.03 (0.78-5.28)				7.85 (4.28-14.40)				2.47 (1.06-5.76)	
Adjusted P value	0.148				<0.001‡				0.037‡	

NS = nephrotic syndrome; OR = odds ratio; CI = confidence interval; NOACs = non-vitamin K antagonist oral anticoagulants; UTI = urinary tract infection; GI = gastrointestinal; NIHSS = national institute of health stroke scale; mRS = modified Rankin scale.

Data are presented as mean  $\pm$  standard deviation, median (interquartile range) or n (%).

\*P < 0.05, Student t test or Mann-Whitney U test; † P < 0.05, Chi-square test; ‡ P < 0.05, adjusted P value using multivariate logistic regression analysis.

