

TITLE PAGE

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**Characteristics of Ischemic Stroke and Intracranial Hemorrhage in Patients with
Nephrotic Syndrome**

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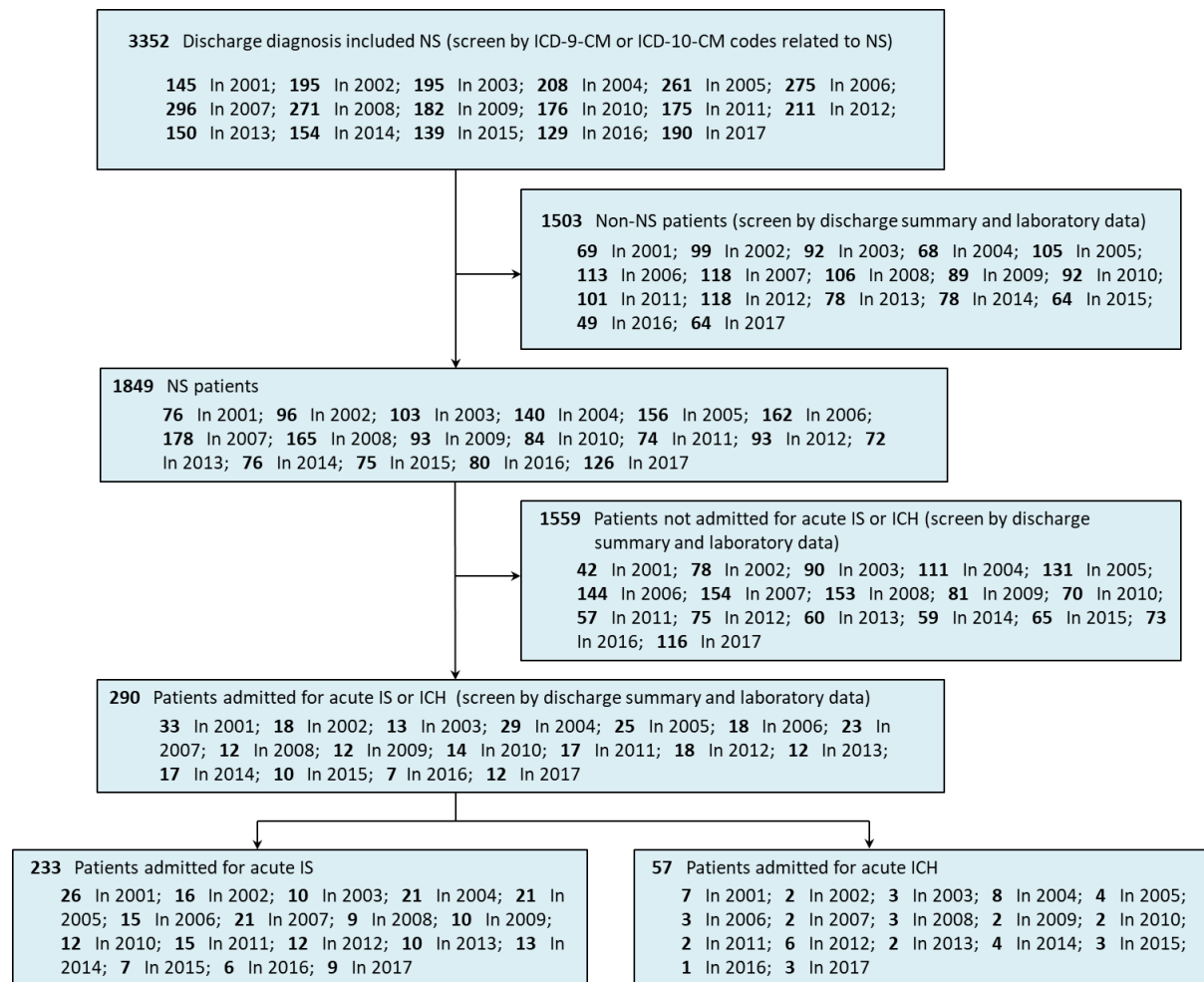
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Supplementary Figure 1. Flow of study selection. NS indicates nephrotic syndrome; IS, ischemic stroke; ICH, intracranial hemorrhage.



Supplementary Table 1. The numbers of missing laboratory data.

	The number of missing data, n (%)	
	Ischemic stroke	Any intracranial hemorrhage
	(n=233)	(n=57)
White blood cells	0 (0)	0 (0)
Hemoglobin	0 (0)	0 (0)
Platelet	0 (0)	0 (0)
INR	10 (4.3)	2 (3.5)
APTT/NC	10 (4.3)	2 (3.5)
High-sensitivity C-reactive protein	21 (9.0)	5 (8.8)
ESR	24 (10.3)	7 (12.2)
Total cholesterol	10 (4.3)	2 (3.5)
Triglyceride	11 (4.7)	2 (3.5)
LDL	17 (7.6)	4 (7.0)
HDL	17 (7.6)	4 (7.0)
Albumin	13 (5.6)	3 (5.3)
Total protein	18 (7.7)	5 (8.8)
Sugar	29 (12.4)	9 (15.8)
Glycohemoglobin	21 (9)	6 (10.5)
BUN	10 (4.3)	2 (3.5)
Creatinine	0 (0)	0 (0)
AST	17 (7.6)	5 (8.8)
ALT	16 (6.9)	5 (8.8)
Uric acid	26 (11.2)	8 (14.0)
Sodium	14 (6.0)	6 (10.5)
Potassium	11 (4.7)	5 (8.8)
Calcium	25 (10.7)	7 (12.3)
Phosphate	29 (12.4)	8 (14.0)

INR indicates international normalized ratio; APTT/NC, activated partial thromboplastin time/normal control; ESR, erythrocyte sedimentation rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine aminotransferase; ANA, antinuclear antibody; VDRL, the venereal disease research laboratory test.

Supplementary Table 2. Demographic features of nephrotic syndrome patients with stroke (additional data).

	Ischemic stroke (n=233)	Any intracranial hemorrhage (n=57)	Odds ratio (95% confidence interval)	P value
Height (cm)	163 (157-168)	165 (158-167)		0.831
Body weight (kg)	63 (58-69)	62 (55-70)		0.828
BMI (kg/m ²)	24.6 (22.7-26.3)	21.1 (19.3-24.8)		0.357
SBP (mmHg)	169 (150-190)	167 (132-192)		0.176
DBP (mmHg)	90 (78-96)	87 (80-102)		0.889
Other diseases				
Chronic obstructive lung disease (%)	12 (9.9)	1 (1.8)	3.04 (0.39-23.9)	0.236
Systemic lupus erythematosus (%)	6 (2.8)	1 (1.8)	1.48 (0.18-12.5)	0.585
End-stage renal disease with dialysis (%)	35 (15)	11 (19.3)	0.74 (0.35-1.56)	0.272
Lab data				
Hemoglobin (mmol/L)	7.39 (6.45-8.25)	7.23 (6.14-8.13)		0.312
Platelet ($\times 10^9$ /L)	214 (170-269)	213 (161-258)		0.801
INR	0.99 (0.90-1.09)	1.09 (0.98-1.20)		0.371
APTT/NC	0.99 (0.92-1.06)	0.99 (0.89-1.04)		0.574
Sugar (mmol/L)	7.9 (6.3-8.6)	6.8 (6.5-8.1)		0.220
Glycohemoglobin (%)	7.7 (6.0-9.4)	7.63 (5.9-8.8)		0.372
ESR (mm/hr)	34.5 (18.3-70.3)	25.5 (13.3-64.8)		0.545
BUN (mmol/L)	8.31 (6.4-19-64)	8.25 (5.07-18.64)		0.063
Creatinine (μ mol/L)	155.47 (106.12-336.21)	153.30 (83.11-308.59)		0.941
AST (μ kat/L)	0.35 (0.25-0.58)	0.31 (0.22-0.52)		0.443
ALT (μ kat/L)	0.32 (0.23-0.61)	0.34 (0.21-0.54)		0.601

LDL (mmol/L)	3.91 (3.11-4.66)	3.88 (2.98-4.69)		0.834
HDL (mmol/L)	1.06 (0.92-1.31)	1.13 (0.93-1.29)		0.394
Uric acid (μ mol/L)	392.5 (303.3-472.3)	386.6 (327.1-469.9)		0.896
Sodium (mmol/L)	138.9 (132.1-146.7)	134.5 (131.5- 145.9)		0.262
Potassium (mmol/L)	4.1 (3.5-4.8)	3.9 (3.3-4.7)		0.361
Calcium (mmol/L)	2.14 (2.09-2.72)	2.16 (2.02-2.64)		0.705
Phosphate (mmol/L)	1.17 (1.13-1.45)	1.15 (1.12-1.45)		0.453
Total protein (g/L)	52 (32-59)	42 (35-50)		0.460
ANA (%)	3 (1.3)	0 (0)	1.01 (1.00-1.03)	0.517
VDRL (%)	4 (1.7)	0 (0)	1.02 (1.00-1.04)	0.415

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; INR, international normalized ratio; APTT/NC, activated partial thromboplastin time/normal control; ESR, erythrocyte sedimentation rate; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ANA, antinuclear antibody; VDRL, the venereal disease research laboratory test.

Data are presented as median (interquartile range) or absolute numbers (percentage).

* $P < 0.05$, Mann-Whitney U test; † $P < 0.05$, Chi-square test.

Supplementary Table 3. Demographic features and clinical courses of nephrotic syndrome patients with ischemic stroke (additional data).

Subtypes	All ischemic stroke (n=233)					<i>P</i> value
	Large-artery atherosclerosis (n=43)	Cardioembolism (n=23)	Small-artery occlusion (n=117)	Stroke of other determined etiology (n=11)	Stroke of undetermined etiology (n=39)	
Height (cm)	162 (158-169)	163 (161-168)	162 (158-169)	166 (158-169)	164 (159-169)	0.654
Body weight (kg)	61 (55-68)	67 (62-71)	64. (55-69)	57 (53-61)	59 (52-64)	0.122
BMI (kg/m ²)	23.8 (22.3-28.1)	25.0 (23.9-25.6)	24.8 (23.2-26.4)	22.1 (19.2-23.1)	23.3 (22.2-25.9)	0.065
SBP (mmHg)	175 (155-181)	160 (130-185)	176 (150-190)	160 (135-171)	170 (155-191)	0.439
DBP (mmHg)	95 (85-100)	88 (78-95)	90 (76-97)	86 (76-96)	90 (75-101)	0.922
Other diseases						
Chronic obstructive lung disease (%)	5 (11.6)	4 (17.4)	2 (1.7)	0 (0)	1 (0.4)	0.005†
Systemic lupus erythematosus (%)	0 (0)	0 (0)	0 (0)	6 (54.5) [†]	0 (0)	<0.001†
End-stage renal disease with dialysis (%)	8 (18.6)	2 (8.7)	17 (14.5)	0 (0)	8 (20.5)	0.400
Clinical syndromes						
TACS (%)	8 (18.6)	6 (26.1)	0 (0)	0 (0)	1 (2.6)	<0.001†
PACS (%)	13 (30.2)	7 (30.4)	19 (16.2)	8 (72.7)	20 (51.3)	<0.001†
LACS (%)	8 (18.6)	4 (17.4)	71 (60.7)	0 (0)	7 (17.9)	<0.001†
POCS (%)	14 (32.6)	6 (26.1)	27 (23.1)	3 (27.3)	10 (25.6)	0.828

Lab data						
WBC ($\times 10^9/L$)	8.32 (6.21-10.25)	7.95 (5.99-9.21)	7.86 (5.76-9.11)	9.12 (6.07-10.11)	8.21 (5.65-9.54)	0.226
Hemoglobin (mmol/L)	7.38 (6.41-8.35)	7.82 (6.52-8.41)	7.45 (6.22-8.35)	7.63 (6.11-8.79)	7.14 (5.99-8.43)	0.442
Platelet ($\times 10^9/L$)	205 (145-330)	231 (160-310)	217 (140-289)	212 (152-320)	220 (155-310)	0.188
INR	0.91 (0.89-1.12)	1.25 (0.98-1.42)	1.10 (0.98-1.31)	1.01 (0.91-1.15)	0.93 (0.89-1.19)	0.066
APTT/NC	1.02 (0.91-1.21)	1.71 (1.41-1.92)	1.11 (0.98-1.13)	1.03 (1.01-1.21)	1.51 (1.31-1.61)	0.068
Sugar (mmol/L)	8.4 (7.3-8.8)	6.7 (5.9-7.6)	8.0 (6.9-8.5)	5.4 (4.9-6.1)	5.7 (5.1-6.4)	0.300
Glycohemoglobin (%)	8.62 (5.92-9.11)	6.83 (5.89-7.23)	8.30 (6.10-8.98)	6.35 (5.87-7.95)	7.61 (5.89-8.91)	0.057
Hs-CRP (nmol/L)	208.57 (44.41-331.52)	137.14 (37.14-241.91)	97.14 (32.14-139.71)	84.76 (24.21-119.25)	141.90 (33.42-221.57)	0.400
ESR (mm/hr)	57.4 (20.3-69.2)	29.2 (10.1-48.7)	43.8 (12.6-66.5)	32.1 (10.8-52.9)	47.6 (15.5-48.7)	0.556
BUN (mmol/L)	9.52 (5.21-18.23)	8.96 (5.00-16.3)	9.75 (4.75-18.92)	8.96 (4.95-14.21)	9.57 (5.56-15.54)	0.933
Creatinine ($\mu\text{mol/L}$)	318.31 (212.12-421.2)	256.42 (189.92-356.1)	265.26 (190.50-366.12)	168.01 (107.12-182.9)	247.58 (115.22-357.23)	0.433
AST ($\mu\text{kat/L}$)	0.33 (0.29-0.59)	0.48 (0.21-0.67)	0.37 (0.20-0.57)	0.27 (0.21-0.52)	0.35(0.25-0.58)	0.100
ALT ($\mu\text{kat/L}$)	0.38 (0.26-0.55)	0.45 (0.33-0.59)	0.40 (0.33-0.59)	0.25 (0.22-0.58)	0.42 (0.32-0.52)	0.408
Total cholesterol (mmol/L)	5.59 (4.13-6.83)	4.54 (4.01-5.87)	5.97 (4.34-6.11)	5.35 (4.25-6.32)	5.12 (4.32-5.99)	0.144
Triglyceride (mmol/L)	1.60 (1.07-2.73)	1.43 (0.91-2.10) [†]	2.29 (1.76-2.89)	2.28 (1.76-2.83)	1.90 (1.45-2.21)	0.025*
LDL (mmol/L)	3.93 (3.10-4.69)	3.18 (2.99-4.56)	4.24 (3.42-4.99)	3.36 (2.70-4.51)	3.98 (2.98-4.91)	0.628
HDL (mmol/L)	1.06 (0.92-1.29)	0.91 (0.88-1.11)	1.03 (0.91-1.31)	1.22 (1.09-1.29)	1.09 (0.99-1.31)	0.628
Uric acid ($\mu\text{mol/L}$)	398.2 (298.2-411.2)	410.4 (299.1-460.3)	380.6 (265.2-398.3)	485.8 (373.1-499.2)	392.5 (279.3-443.1)	0.490

Sodium (mmol/L)	131.6 (130.2-138.5)	133.4 (129.3-139.2)	132.9 (129.5-136.9)	137.9 (132.9-141.6)	134.9 (132.7-140.6)	0.821
Potassium (mmol/L)	3.8 (3.5-4.3)	3.9 (3.5-4.5)	3.8 (3.4-4.2)	4.2 (3.4-4.9)	4.0 (3.5-4.6)	0.824
Calcium (mmol/L)	2.14 (2.09-2.72)	2.11 (1.99-2.67)	1.99 (1.96-2.76)	1.92 (1.91-2.11)	2.12(1.98-2.32)	0.900
Phosphate (mmol/L)	1.18 (1.13-1.55)	0.99 (0.96-0.1.66)	1.10 (0.95-1.94)	1.06 (0.89-2.10)	1.01 (0.91-2.02)	0.921
Albumin (g/L)	22 (19-29)	20 (17-28)	21 (19-29)	18 (15-24)	22 (18-31)	0.876
Total protein, g/L	52 (39-56)	41 (35-55)	38 (33-51)	32 (21-49)	49 (31-59)	0.425
ANA (%)	0 (0)	0 (0)	0 (0)	6 (54.5) [†]	0 (0)	<0.001 [‡]
VDRL (%)	0 (0)	0 (0)	1 (0.9)	2 (18.2) [†]	1 (2.6)	0.001 [‡]
Fibrinogen (g/L)	4.73 (3.56-5.87)	7.32 (6.74-8.31)	3.97 (2.99-4.12)	3.42 (3.31-4.22)	4.65 (3.73-5.21)	0.084
Homocysteine (μmol/L)	11.9 (8.9-14.2)	14.6 (12.3-16.9)	12.3 (112.2-130.1)	9.7 (8.9-11.2)	13.0 (12.7-14.3)	0.707
Protein S (%)	121.2 (106.6-131.9)	118.1 (106.4-124.2)	99.1 (87.9-111.2)	104.0 (99.1-115.8)	120.0 (116.1-134.1)	0.083
Protein C (%)	120.7 (113.2-127.1)	115.2 (106.1-124.4)	117.6 (108.2-125.6)	103.8 (106.1-121.2)	107.1 (103.2-122.4)	0.547
Left ventricular ejection fraction (%)	58.2 (49.6-68.5)	58.5 (48.4-59.5)	61.2 (50.4-72.1)	55.1 (49.5-62.1)	58.4 (50.3-66.2)	0.215
Complication at admission						
Other infection (%)	7 (16.3)	1 (4.3)	5 (4.3)	1 (9.1)	3 (7.7)	0.132
Acute coronary syndrome (%)	1 (2.3)	1 (4.3)	0 (0)	0 (0)	1 (2.6)	0.376
Venous thromboembolism (%)	1 (2.3)	1 (4.3)	0 (0)	0 (0)	0 (0)	0.213
Pulmonary edema (%)	4 (9.3)	3 (13)	4 (3.4)	0 (0)	2 (5.1)	0.261
Glasgow coma scale score						

Upon admission	15 (15-15)	15 (13-15)	15 (15-15)	15 (15-15)	15 (15-15)	<0.001*
Upon discharge	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)	15 (15-15)	<0.001*
modified Rankin scale score						
Upon admission	4 (3-5)	3 (3-4)	3 (2-3)	2 (2-4)	3 (3-5)	<0.001*
Upon discharge	4 (3-5)	3 (3-5)	3 (2-3)	2 (2-4)	3 (3-4)	<0.001*

BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; 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; AST, aspartate transaminase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ANA, antinuclear antibody; VDRL, the venereal disease research laboratory test.

Data are presented as median (interquartile range) or absolute numbers (percentage).

* $P < 0.05$, Kruskal-Wallis test; † $P < 0.05$, Chi-square test.

Supplementary Table 4. Demographic features and clinical courses of nephrotic syndrome patients with intracranial hemorrhage (additional data).

Types of hemorrhage	Intracerebral hemorrhage (n=45)	Any intracranial hemorrhage (n=57)			<i>P</i> value
		Subarachnoid hemorrhage (n=4)	Subdural hemorrhage (n=7)	Arteriovenous malformation (n=1)	
Location of hemorrhage (patients)	Cerebral hemisphere: 10, basal ganglia: 20, brainstem: 8, cerebellum: 7				
Complication at admission					
Pneumonia (%)	9 (20)	1 (25)	1(14.3)	0 (0)	0.930
Gastrointestinal bleeding (%)	8 (17.8)	1 (25)	0 (0)	0 (0)	0.596
Urinary tract infection (%)	10 (22.2)	2 (50)	1 (14.3)	0 (0)	0.518
Other infection (%)	2 (4.4)	0 (0)	0 (0)	0 (0)	0.907
Acute coronary syndrome (%)	1 (2.2)	0 (0)	0 (0)	0 (0)	0.965
Venous thromboembolism (%)	1 (2.2)	0 (0)	0 (0)	0 (0)	0.965
Pulmonary edema (%)	1 (2.2)	0 (0)	0 (0)	0 (0)	0.965

Data are presented as absolute numbers (percentage).

* $P < 0.05$, Chi-square test.

Supplementary Table 5. Cox regression analysis of patient survival during the 30-day period, intracranial hemorrhage vs. ischemic stroke (detailed items).

	Univariate Cox regression		Multivariate Cox regression	
	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Age	1.01 (0.98-1.04)	0.610		
Male	0.67 (0.29-1.58)	0.364		
Hypertension	1.21 (0.36-4.10)	0.762		
Diabetes mellitus	0.96 (0.40-2.33)	0.936		
Hyperlipidemia	0.22 (0.08-0.60)	0.003*		
Coronary artery disease	3.12 (1.26-7.72)	0.014*	4.19 (1.67-10.46)	0.002†
Congestive heart failure	2.58 (1.00-6.65)	0.050*		
Atrial fibrillation	1.00 (0.23-4.28)	0.996		
Old stroke	1.05 (0.43-2.61)	0.912		
Smoking	0.57 (0.08-4.25)	0.583		
End-stage renal disease with dialysis	2.20 (0.85-5.67)	0.103		
Pneumonia	3.66 (1.54-8.68)	0.003*		
Intracranial hemorrhage	7.33 (3.04-17.70)	<0.001*	10.68 (3.31-34.47)	<0.001†
Total anterior circulation syndrome	4.82 (1.62-14.34)	0.005*	17.65 (4.37-71.23)	<0.001†

HR indicates hazard ratio; CI, confidence interval.

* $P < 0.1$ for the univariate Cox regression, and † $P < 0.05$ for the multivariate Cox regression.

Supplementary Table 6. Cox regression analysis of patient survival during the 30-day period in nephrotic syndrome patients with ischemic stroke (detailed items).

Variables	Univariate Cox regression, HR (95% CI)	<i>P</i> value	Multivariate Cox regression, HR (95% CI)	<i>P</i> value
Age	0.98 (0.94-1.03)	0.524		
Male	1.85 (0.37-9.17)	0.451		
Hypertension	0.58 (0.12-2.88)	0.506		
Diabetes mellitus	0.88 (0.21-3.69)	0.864		
Hyperlipidemia	0.18 (0.04-0.91)	0.037*		
Coronary artery disease	3.50 (0.84-14.64)	0.086*	24.58 (1.48-408.90)	0.026†
Congestive heart failure	3.83 (0.92-16.02)	0.066*		
Atrial fibrillation	1.33 (0.16-10.82)	0.789		
Hyperuricemia	0.68 (0.08-5.55)	0.721		
Old stroke	0.28 (0.04-2.30)	0.238		
Smoking	1.37 (0.17-11.17)	0.766		
TACS	16.41 (4.10-65.72)	<0.001*		
Pneumonia	8.34 (1.99-34.92)	0.004*		
Gastrointestinal bleeding	3.42 (0.69-16.96)	0.132		
Hemoglobin	0.82 (0.61-1.09)	0.161		
Hs-CRP	1.04 (1.02-1.06)	<0.001*		
Platelet	1.00 (0.99-1.01)	0.792		
Albumin	1.26 (0.73-2.18)	0.413		

HR indicates hazard ratio; CI, confidence interval; TACS, total anterior circulation syndrome; hs-CRP, high-sensitivity C-reactive protein.

* $P < 0.1$ for the univariate Cox regression, and † $P < 0.05$ for the multivariate Cox regression.

Supplementary Table 7. Cox regression analysis of patient survival during the 30-day period in nephrotic syndrome patients with intracranial hemorrhage (detailed items).

Variables	Univariate Cox regression, HR (95% CI)	<i>P</i> value	Multivariate Cox regression, HR (95% CI)	<i>P</i> value
Age	1.04 (0.99-1.08)	0.120		
Male	0.37 (0.12-1.12)	0.078*		
Hypertension	2.88 (0.37-22.13)	0.310		
Diabetes mellitus	1.54 (0.50-4.71)	0.448		
Hyperlipidemia	0.65 (0.18-2.37)	0.516		
Coronary artery disease	3.93 (1.20-12.85)	0.023*	5.49 (1.54-19.56)	0.009†
Congestive heart failure	1.98 (0.54-7.20)	0.301		
Atrial fibrillation	1.13 (0.15-8.66)	0.909		
Hyperuricemia	1.00 (0.13-7.69)	1.00		
Old stroke	2.42 (0.81-7.21)	0.112		
Intracerebral hemorrhage	0.96 (0.27-3.50)	0.955		
Subarachnoid hemorrhage	4.23 (1.15-15.52)	0.030*	6.32 (1.57-25.53)	0.010†
Smoking	0.05 (0.00-455.3)	0.734		
Pneumonia	1.91 (0.59-6.19)	0.284		
Gastrointestinal bleeding	0.89 (0.20-4.00)	0.875		
Hemoglobin	0.85 (0.66-1.09)	0.195		
Hs-CRP	1.00 (0.98-1.02)	0.812		
Platelet	1.00 (1.00-1.01)	0.157		
Albumin	0.98 (0.67-1.44)	0.925		

HR indicates hazard ratio; CI, confidence interval; hs-CRP, high-sensitivity C-reactive protein.

* $P < 0.1$ for the univariate Cox regression, and † $P < 0.05$ for the multivariate Cox regression.