

Supplementary Material

Supplement table 1. Baseline characteristics of participants by NSE level

Index	Normal NSE (N=351)	High NSE (N=80)	Standardize diff.	P-value
Basic information				
Sex (men) (%)	185 (52.71)	47 (58.75)	0.12 (-0.12, 0.36)	0.328
Age (years)	72.36 ± 10.61	76.09 ± 11.39	0.34 (0.09, 0.58)	0.005
Disease duration (hours)	7.00 (3.75-18.00)	7.00 (4.88-15.88)	0.08 (-0.16, 0.33)	0.960
OCSP classification				
TACI (%)	38 (10.83)	10 (12.50)	0.05 (-0.19, 0.30)	0.668
PACI (%)	103 (29.34)	28 (35.00)	0.12 (-0.12, 0.36)	0.321
POCI (%)	72 (20.51)	10 (12.50)	0.22 (-0.03, 0.46)	0.099
LACI (%)	138 (39.32)	32 (40.00)	0.01 (-0.23, 0.26)	0.910
Medical history				
Hypertension (%)	308 (87.75)	74 (92.50)	0.16 (-0.08, 0.40)	0.227
Diabetes (%)	124 (35.33)	25 (31.25)	0.09 (-0.16, 0.33)	0.489
CHD (%)	90 (25.64)	29 (36.25)	0.23 (-0.01, 0.47)	0.055
Atrial fibrillation (%)	9 (2.56)	5 (6.25)	0.18 (-0.06, 0.42)	0.093
Blood routine indicators				
Leukocyte count (10 ¹² /L)	6.93 ± 2.09	7.50 ± 2.12	0.27 (0.03, 0.51)	0.030
RBC (10 ¹² /L)	4.40 ± 0.60	4.38 ± 0.75	0.03 (-0.21, 0.27)	0.807
Platelet (10 ⁹ /L)	217.48 ± 64.75	232.28 ± 84.89	0.20 (-0.05, 0.44)	0.084
Hemoglobin (g/L)	128.45 ± 19.71	127.66 ± 26.30	0.03 (-0.21, 0.28)	0.763
Blood biochemical indicators				
ALT (U/L)	17.30 (12.25-24.30)	16.05 (11.35-20.90)	0.15 (-0.09, 0.40)	0.250
Total bilirubin (μmol/L)	11.80 (8.50-15.60)	12.40 (9.30-18.45)	0.31 (0.06, 0.55)	0.002
Total protein (g/L)	68.48 ± 7.65	68.95 ± 9.34	0.05 (-0.19, 0.30)	0.636
Albumin (g/L)	40.35 ± 4.89	40.10 ± 6.18	0.05 (-0.20, 0.29)	0.693
Uric acid (μmol/L)	288.55 ± 100.71	299.82 ± 122.81	0.10 (-0.14, 0.34)	0.387
Creatinine (μmol/L)	76.45 ± 30.31	94.69 ± 61.15	0.38 (0.13, 0.62)	0.032

BUN (mmol/L)	5.50 (4.50-6.70)	5.55 (4.40-6.93)	0.34 (0.10, 0.59)	<0.001
HCY (μ mol/L)	13.00 (8.00-20.00)	16.00 (8.75-25.25)	0.29 (0.05, 0.54)	0.078
ESR (mm/h)	22.00 (11.00-30.00)	20.50 (11.75-26.25)	0.02 (-0.23, 0.26)	0.545
LDL-C (mmol/L)	2.80 \pm 0.97	3.01 \pm 1.00	0.21 (-0.03, 0.46)	0.085
HDL-C (mmol/L)	1.24 \pm 0.32	1.28 \pm 0.42	0.10 (-0.14, 0.34)	0.383
TG (mmol/L)	1.36 \pm 0.94	1.35 \pm 0.70	0.01 (-0.23, 0.25)	0.934
TCH (mmol/L)	4.43 \pm 1.06	4.64 \pm 1.10	0.19 (-0.05, 0.44)	0.113
Fasting glucose (mmol/L)	6.05 \pm 1.82	6.24 \pm 1.99	0.10 (-0.14, 0.34)	0.408
NSE (ng/mL)	12.41 \pm 2.17	18.69 \pm 2.11	2.94 (2.62, 3.25)	<0.001
Clotting index				
D-dimer (ug/ml)	0.38 (0.22-0.80)	0.43 (0.27-1.18)	0.12 (-0.13, 0.36)	0.080
PT (second)	10.92 \pm 0.77	11.31 \pm 1.24	0.38 (0.13, 0.62)	<0.001
PTT (second)	27.36 \pm 3.78	28.57 \pm 4.24	0.30 (0.06, 0.54)	0.012
Fibrinogen (g/L)	2.88 \pm 0.79	3.27 \pm 0.88	0.47 (0.22, 0.71)	<0.001
Tumor index				
AFP (ng/ml)	1.90 (1.00-2.85)	1.60 (0.70-2.60)	0.11 (-0.13, 0.36)	0.170
CEA (ng/ml)	1.52 (0.91-2.33)	1.33 (0.85-2.37)	0.07 (-0.18, 0.31)	0.292
CA153 (u/ml)	7.40 (6.00-10.60)	8.05 (5.77-13.37)	0.14 (-0.10, 0.39)	0.298
CA724 (u/ml)	1.81 (1.07-3.87)	2.30 (1.58-5.94)	0.14 (-0.10, 0.38)	0.007
Medication use before admission				
Antihypertensive drugs (%)	290 (82.62)	70 (87.50)	0.14 (-0.11, 0.38)	0.288
Lipid lowering drugs (%)	135 (38.46)	34 (42.50)	0.08 (-0.16, 0.33)	0.504
Antidiabetic drugs (%)	116 (33.05)	23 (28.75)	0.09 (-0.15, 0.34)	0.458
Antiplatelet drugs (%)	300 (85.47)	69 (86.25)	0.02 (-0.22, 0.27)	0.858

AFP: Alpha-fetoprotein, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, CEA: Carcinoembryonic antigen, CA: Cancer, CHD: Coronary heart disease, ESR: Erythrocyte sedimentation rate, HCY: Hemocyanin, HDL-C: High density lipoprotein cholesterol, INR: International normalized ratio, LACI: Lacunar infarction, LDL-C: Low density lipoprotein, NSE: Neuron-specific enolase, OCSF: Oxfordshire community stroke project, PACI: Partial anterior circulation infarction, POCI: posterior circulation infarction, PT: Prothrombin time, PTT: Partial thromboplastin time, RBC: Red blood cell, TACI: Total anterior circulation infarction, TCH: Total cholesterol, TG: Triglyceride.

Supplement table 2. Baseline characteristics of participants by fibrinogen level

Index	Normal fibrinogen group (N=388)	High fibrinogen group (N=43)	Standardize diff	P-value
Basic information				
Sex (men) (%)	209 (53.87)	23 (53.49)	0.01 (-0.31, 0.32)	0.962
Age (years)	72.55±10.93	77.58±8.94	0.50 (0.19, 0.82)	0.004
Disease duration (hours)	7.00 (3.88-17.25)	8.00 (5.50-17.50)	0.10 (-0.22, 0.41)	0.185
OCSP classification				
TACI (%)	45 (11.60)	3 (6.98)	0.16 (-0.16, 0.47)	0.361
PACI (%)	114 (29.38)	17 (39.53)	0.21 (-0.10, 0.53)	0.170
POCI (%)	75 (19.33)	7 (16.28)	0.08 (-0.24, 0.39)	0.629
LACI (%)	154 (39.69)	16 (37.21)	0.05 (-0.26, 0.37)	0.752
Medical history				
Hypertension (%)	342 (88.14)	40 (93.02)	0.17 (-0.15, 0.48)	0.339
Diabetes (%)	133 (34.28)	16 (37.21)	0.06 (-0.25, 0.38)	0.701
CHD (%)	103 (26.55)	16 (37.21)	0.23 (-0.09, 0.55)	0.138
Atrial fibrillation (%)	13 (3.35)	1 (2.33)	0.06 (-0.25, 0.38)	0.719
Blood routine indicators				
Leukocyte count (10 ¹² /L)	6.87±1.98	8.59±2.61	0.74 (0.42, 1.06)	<0.001
Women (10 ¹² /L)	6.82±2.07	8.43±3.09	0.61 (0.14, 1.08)	0.002
Men (10 ¹² /L)	6.91±1.89	8.73±2.17	0.89 (0.46, 1.33)	<0.001
High leukocyte (%)	25 (6.44)	16 (37.21)	0.80 (0.48, 1.12)	<0.001
Neutrophil count (10 ⁹ /L)	4.43±1.73	6.37±3.13	0.77 (0.45, 1.09)	<0.001
Monocyte count (10 ⁹ /L)	0.41 (0.34-0.52)	0.46 (0.34-0.68)	0.49 (0.17, 0.80)	0.018
Lymphocyte count (10 ⁹ /L)	1.73 (1.36-2.30)	1.57 (1.36-2.26)	0.09 (-0.23, 0.40)	0.421
RBC (10 ¹² /L)	4.41±0.62	4.29±0.71	0.18 (-0.14, 0.49)	0.238
Platelet (10 ⁹ /L)	215.94±65.0	258.95±90.43	0.55 (0.23, 0.86)	<0.001
Hemoglobin (g/L)	128.96±20.42	122.37±25.58	0.28 (-0.03, 0.60)	0.051
Blood biochemical indicators				

ALT (U/L)	16.65 (12.00-24.33)	18.00 (11.75-21.10)	0.00 (-0.31, 0.32)	0.711
Total bilirubin (µmol/L)	11.85 (8.80-15.60)	13.00 (8.00-17.90)	0.23 (-0.08, 0.55)	0.662
Total protein (g/L)	68.62±7.96	68.08±8.22	0.07 (-0.25, 0.38)	0.674
Albumin (g/L)	40.52±5.12	38.35±5.0	0.43 (0.11, 0.75)	0.008
Uric acid (µmol/L)	292.23±101.30	276.37±135.27	0.13 (-0.18, 0.45)	0.349
Creatinine (µmol/L)	79.70±38.26	81.08±41.42	0.03 (-0.28, 0.35)	0.823
BUN (mmol/L)	5.40 (4.50-6.60)	6.40 (4.75-7.10)	0.28 (-0.03, 0.60)	0.073
HCY (µmol/L)	13.00 (8.00-20.00)	14.00 (10.00-18.50)	0.00 (-0.31, 0.32)	0.606
ESR (mm/h)	21.50 (11.00-29.00)	26.00 (15.00-34.50)	0.33 (0.01, 0.64)	0.059
LDL-C (mmol/L)	2.83±0.98	2.88±0.93	0.04 (-0.27, 0.36)	0.794
HDL-C (mmol/L)	1.25±0.34	1.26±0.35	0.04 (-0.28, 0.35)	0.815
TG (mmol/L)	1.36±0.91	1.28±0.77	0.10 (-0.22, 0.42)	0.560
TCH (mmol/L)	4.47±1.08	4.44±0.96	0.03 (-0.28, 0.35)	0.845
Fasting glucose (mmol/L)	6.11±1.89	5.86±1.49	0.15 (-0.17, 0.46)	0.400
NSE (ng/mL)	13.51±3.17)	14.19±3.99	0.19 (-0.12, 0.51)	0.190
Clotting index				
D-dimer (ug/ml)	0.38 (0.22-0.80)	0.72 (0.45-1.48)	0.33 (0.01, 0.64)	<0.001
PT (second)	10.97±0.83	11.27±1.25	0.28 (-0.03, 0.60)	0.034
PTT (second)	27.41±3.81	29.10±4.33	0.42 (0.10, 0.73)	0.007
Fibrinogen (g/L)	2.75±0.58	4.71±0.48	3.66 (3.26, 4.06)	<0.001
Women (g/L)	2.86±0.60	4.64±0.40	3.47 (2.90, 4.05)	<0.001
Men (g/L)	2.66±0.55	4.77±0.54	3.86 (3.30, 4.41)	<0.001
Tumor index				
AFP (ng/ml)	1.80 (1.00-2.82)	1.50 (0.65-2.50)	0.35 (0.03, 0.66)	0.100
CEA (ng/ml)	1.46 (0.88-2.24)	1.96 (1.11-2.45)	0.05 (-0.26, 0.37)	0.088
CA153 (u/ml)	7.50 (6.00-10.60)	8.00 (5.30-12.70)	0.24 (-0.07, 0.56)	0.554
CA724 (u/ml)	1.98 (1.11-3.97)	2.03 (1.09-6.02)	0.03 (-0.28, 0.35)	0.487
Medication use before admission				
Antihypertensive drugs (%)	324 (83.51)	36 (83.72)	0.01 (-0.31, 0.32)	0.971

Lipid lowering drugs (%)	148 (38.14)	21 (48.84)	0.22 (-0.10, 0.53)	0.173
Antidiabetic drugs (%)	123 (31.70)	16 (37.21)	0.12 (-0.20, 0.43)	0.463
Antiplatelet drugs (%)	330 (85.05)	39 (90.70)	0.17 (-0.14, 0.49)	0.317

AFP: Alpha-fetoprotein, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, CEA: Carcinoembryonic antigen, CA: Cancer, CHD: Coronary heart disease, ESR: Erythrocyte sedimentation rate, HCY: Hemocyanin, HDL-C: High density lipoprotein cholesterol, INR: International normalized ratio, LACI: Lacunar infarction, LDL-C: Low density lipoprotein, NSE: Neuron-specific enolase, OCSF: Oxfordshire community stroke project, PACI: Partial anterior circulation infarction, POCI: posterior circulation infarction, PT: Prothrombin time, PTT: Partial thromboplastin time, RBC: Red blood cell, TACI: Total anterior circulation infarction, TCH: Total cholesterol, TG: Triglyceride.

Supplement Table 3. Characteristics of AIS and healthy control groups after propensity score matching by sex and age

Characteristic	Healthy control (N=89)	AIS (N=89)	Standardize diff	P-value
Basic information				
Sex (men) (%)	36(40.45)	41(46.07)	0.11(-0.18,0.41)	0.449
Age (years)	68.31±9.01	67.75±10.79	0.06(-0.24,0.35)	0.707
Laboratory tests				
Leukocyte count (10 ¹² /L)	6.11±1.81	7.27±2.36	0.55(0.25,0.85)	<0.001
Fibrinogen (g/L)	2.66±0.65	2.94±0.81	0.38(0.08,0.68)	0.012
NSE (ng/mL)	12.79±3.70	14.07±3.13	0.37 (0.08, 0.67)	0.014
Medical history				
Hypertension (%)	/	76(85.39)	/	/
Diabetes (%)	/	34(38.20)	/	/
CHD (%)	/	15(16.85)	/	/
Atrial fibrillation (%)	/	0 (0.00)	/	/

AIS: acute ischemic stroke, CHD: coronary heart disease

Supplement Table 4. Hierarchical analysis on relationship of leukocyte and high NSE

Hierarchical factor		N	OR (95% CI) <i>p</i>	<i>p</i> for interaction
Sex (%)	Women	199	1.09 (0.90, 1.32) 0.369	0.273
	Men	232	1.26 (1.05, 1.51) 0.011	
Age (years)	<75	239	1.21 (1.01, 1.46) 0.041	0.293
	≥75	192	1.06 (0.90, 1.25) 0.483	
CHD (%)	No	312	1.17 (1.01, 1.35) 0.041	0.552
	Yes	119	1.07 (0.85, 1.36) 0.563	
RBC (10 ¹² /L)	<5.0	366	1.08 (0.94, 1.24) 0.270	0.193
	≥5.0	65	1.36 (0.98, 1.87) 0.065	
Creatinine (μmol/L)	<72	215	1.16 (1.02, 1.32) 0.020	0.719
	≥72	216	1.01 (0.48, 2.13) 0.982	
BUN (mmol/L)	<5.50	209	1.21 (1.00, 1.46) 0.045	0.537
	≥5.50	221	1.12 (0.95, 1.32) 0.170	
HCY (μmol/L)	<15.0	229	1.16 (0.99, 1.36) 0.065	0.642
	≥15.0	202	1.10 (0.94, 1.29) 0.225	
LDL-C (mmol/L)	<3.10	272	1.16 (0.99, 1.36) 0.074	0.763
	≥3.10	159	1.11 (0.92, 1.35) 0.267	
Fasting glucose (mmol/L)	<6.10	275	1.12 (0.95, 1.30) 0.168	0.563
	≥6.10	156	1.21 (0.97, 1.50) 0.090	

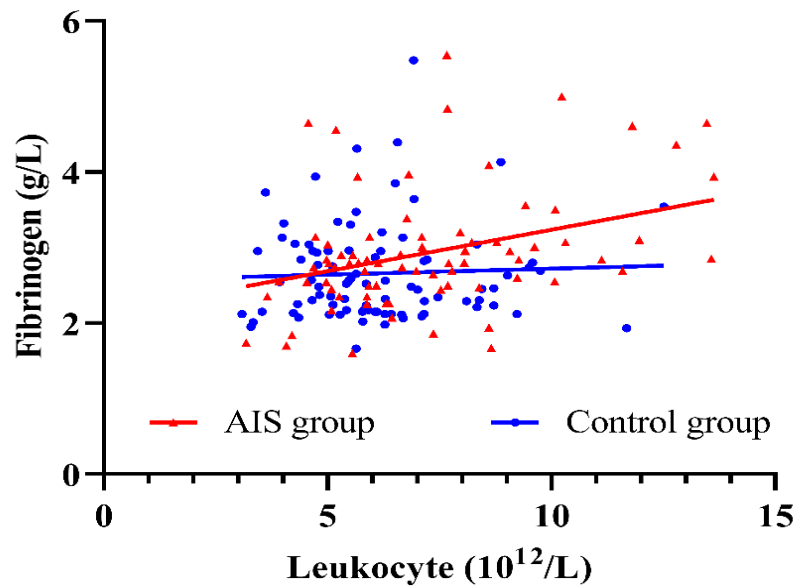
Each stratification adjusted for all the factors (sex, age, CHD, RBC, creatinine, BUN, HCY, LDL-C, fasting glucose) except the stratification factor itself.

Supplement Table 5. Hierarchical analysis on relationship of leukocyte and high fibrinogen

Hierarchical factor		N	OR (95% CI) <i>p</i>	<i>p</i> for interaction
Sex (%)	Women	199	1.29 (1.01, 1.64) 0.038	0.419
	Men	232	1.47 (1.18, 1.85) <0.001	
Age (years)	<75	239	1.32 (1.03, 1.70) 0.027	0.817
	≥75	192	1.37 (1.13, 1.67) 0.001	
Diabetes (%)	No	282	1.34 (1.09, 1.65) 0.005	0.299
	Yes	149	1.63 (1.19, 2.22) 0.002	
Lymphocyte count (10 ⁹ /L)	<1.73	214	1.50 (1.20, 1.89) <0.001	0.481
	≥1.73	217	1.33 (1.04, 1.71) 0.024	
Platelets (10 ⁹ /L)	<209	215	1.56 (1.18, 2.07) 0.001	0.273
	≥209	216	1.29 (1.06, 1.57) 0.010	
ALT (U/L)	<16.90	215	1.29 (1.03, 1.62) 0.027	0.493
	≥16.90	216	1.44 (1.15, 1.81) 0.001	
BUN (mmol/L)	<5.50	209	1.53 (1.15, 2.03) 0.003	0.467
	≥5.50	221	1.34 (1.11, 1.62) 0.002	
LDL-C (mmol/L)	<3.10	272	1.40 (1.15, 1.70) 0.001	0.668
	≥3.10	159	1.30 (0.97, 1.73) 0.079	
Fasting glucose (mmol/L)	<6.10	275	1.25 (1.03, 1.52) 0.021	0.078
	≥6.10	156	1.79 (1.23, 2.60) 0.002	
Lipid lowering drugs (%)	No	262	1.29 (1.03, 1.60) 0.025	0.334
	Yes	169	1.50 (1.18, 1.92) 0.001	
Antiplatelet drugs (%)	No	62	1.21 (0.77, 1.89) 0.409	0.601
	Yes	369	1.37 (1.16, 1.63) <0.001	

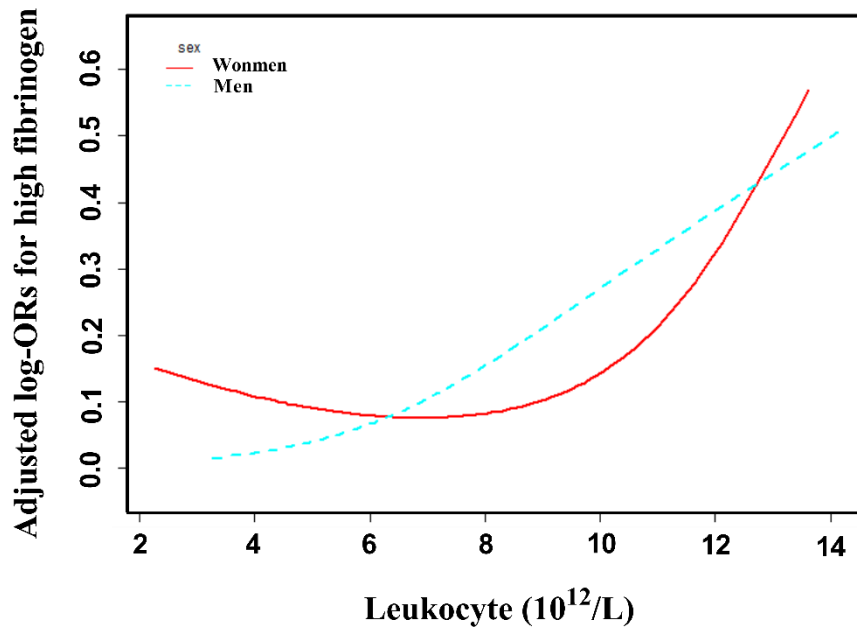
Each stratification adjusted for all the factors (sex, age, diabetes, lymphocyte count, platelet, ALT, BUN, LDL-C, fasting glucose, lipid lowering drugs, and antiplatelet drugs) except the stratification factor itself.

Supplement figure 1.



Person's correlation between leukocyte and fibrinogen in the AIS and healthy control groups, respectively. The Person's correlation coefficient (95%) for the relationship between leukocytes and fibrinogen were 0.321 (0.121-0.496, $p=0.002$) in the matched AIS group, and 0.045 (-0.165-0.251, $p=0.676$) in the healthy control group. Which showed that the level of fibrinogen was observed increasing with the elevated level of leukocyte in the matched AIS group, but not in the healthy control group.

Supplement figure 2.



Linear curve fitting of the relationship between leukocyte and high fibrinogen. A hierarchical analysis by sex showed linear relationships between leukocyte and high fibrinogen in women ($p=0.027$) and men ($p<0.001$) after adjusting for sex, age, diabetes, lymphocyte count, platelet, ALT, BUN, LDL-C, fasting glucose, lipid lowering drugs, and antiplatelet drugs, respectively.