Supplementary material

Figure S1. Study Population.

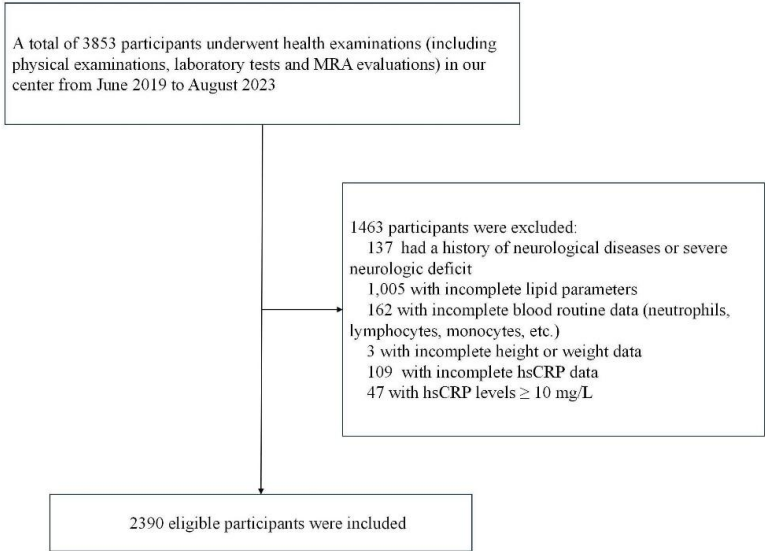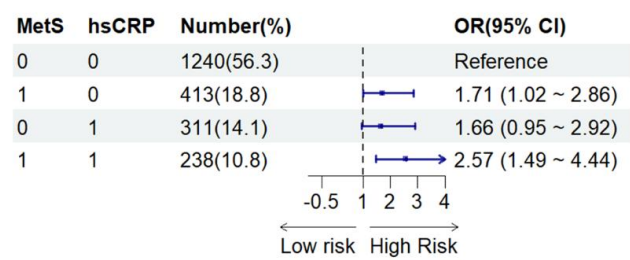| MetS	hsCRP	Number(%)		OR(95% CI)
0	0	1240(56.3)		Reference
1	0	413(18.8)		1.71 (1.02 ~ 2.86)
0	1	311(14.1)		1.66 (0.95 ~ 2.92)
1	1	238(10.8)		2.57 (1.49 ~ 4.44)

-0.5 1 2 3 4

Low risk   High Risk

Figure S2: Joint effects of hsCRP and MetS on aICAS in the subgroup aged ≤ 65 years. The groups are defined as follows: 00- no metabolic syndrome, hsCRP in quartiles 1-3; 10-metabolic syndrome present, hsCRP in quartiles 1-3; 01- no metabolic syndrome, hsCRP in quartile 4; 11- metabolic syndrome present, hsCRP in quartile 4. Adjusted for sex and coronary heart disease. OR, odds ratio; CI, confidence interval; MetS, metabolic syndrome; aICAS, asymptomatic intracranial arterial stenosis; hsCRP, high-sensitivity C-reactive protein.

Table S1: Baseline characteristics of the participants aged over or not greater than 65 years old

Characteristics	Total (n = 2390)	Participants aged ≤ 65s (n = 2202)	Participants aged > 65s (n = 188)	P
Age, year	52.00 (44.00, 58.00)	51.00 (43.00, 56.00)	69.00 (67.00, 72.00)	<0.001
Male, n (%)	1469 (61.46)	1371 (62.26)	98 (52.13)	0.006
BMI, kg/㎡	25.40 (23.19, 27.76)	25.39 (23.18, 27.75)	25.57 (23.55, 27.87)	0.533
Hypertension, n (%)	623 (26.07)	543 (24.66)	80 (42.55)	<0.001
Diabetes mellitus, n (%)	223 (9.33)	193 (8.76)	30 (15.96)	0.001
Coronary heart disease, n (%)	69 (2.89)	56 (2.54)	13 (6.91)	<0.001
Dyslipidemia, n (%)	217 (9.08)	194 (8.81)	23 (12.23)	0.117
Smoking, n (%)	714 (29.87)	660 (29.97)	54 (28.72)	0.719
TC, mmol/l	4.89 (4.30, 5.49)	4.88 (4.29, 5.49)	4.94 (4.33, 5.52)	0.652
LDL-C, mmol/l	3.05 (2.46, 3.60)	3.04 (2.46, 3.59)	3.09 (2.50, 3.64)	0.497
ApoA1, g/l	1.41 (1.26, 1.57)	1.41 (1.26, 1.57)	1.43 (1.29, 1.58)	0.272
ApoB, g/l	0.93 (0.80, 1.09)	0.93 (0.80, 1.09)	0.94 (0.81, 1.09)	0.517
Hcy, umol/l	12.21 (10.21, 14.94)	12.09 (10.16, 14.80)	13.18 (10.95, 16.56)	<0.001
hsCRP, mg/l	0.72 (0.34, 1.50)	0.69 (0.33, 1.45)	1.10 (0.54, 2.09)	<0.001
NLR	1.94 (1.54, 2.46)	1.93 (1.53, 2.45)	2.03 (1.63, 2.66)	0.052
MHR	0.24 (0.17, 0.31)	0.24 (0.17, 0.31)	0.24 (0.18, 0.31)	0.839
UA, umol/l	341.05 (277.40, 404.48)	341.75 (277.10, 404.65)	322.20 (278.70, 397.85)	0.292
aICAS, n (%)	135 (5.65)	109 (4.95)	26 (13.83)	<0.001
MetS- related characteristics				
Waistline, cm	88.00 (80.00, 94.00)	87.00 (80.00, 94.00)	90.00 (83.00, 94.25)	0.016
SBP, mmHg	127.00 (116.00, 138.00)	126.00 (116.00, 136.00)	141.00 (128.00, 153.00)	<0.001
DBP, mmHg	81.00 (73.00, 89.00)	81.00 (73.00, 89.00)	82.00 (73.75, 88.00)	0.979
HDL-C, mmol/l	1.33 (1.15, 1.55)	1.33 (1.14, 1.56)	1.35 (1.17, 1.54)	0.561
TG, mmol/l	1.33 (0.92, 1.98)	1.34 (0.92, 2.00)	1.27 (0.87, 1.86)	0.095

Table S1: Baseline characteristics of the participants aged over or not greater than 65 years old

Characteristics	Total (n = 2390)	Participants aged ≤ 65s (n = 2202)	Participants aged > 65s (n = 188)	*P*
FBG, mmol/l	4.94 (4.61, 5.45)	4.92 (4.60, 5.40)	5.16 (4.82, 5.86)	<0.001
Metsss	1.22 (0.09, 2.82)	1.12 (0.00, 2.78)	1.86 (0.88, 2.95)	<0.001
Metabolic Syndrome (No. of Components)				<0.001
0	501 (20.96)	492 (22.34)	9 (4.79)	
1	551 (23.05)	509 (23.12)	42 (22.34)	
2	612 (25.61)	550 (24.98)	62 (32.98)	
3	459 (19.21)	408 (18.53)	51 (27.13)	
4	225 (9.41)	206 (9.36)	19 (10.11)	
5	42 (1.76)	37 (1.68)	5 (2.66)	

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL- C, high-density lipoprotein cholesterol; LDL- C, low- density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; Hcy, homocysteine; hsCRP, high-sensitivity C-reactive protein; NLR, neutrophil-lymphocyte ratio; MHR, monocyte-to-high-density lipoprotein-cholesterol ratio; UA, uric acid; MetS, metabolic syndrome; Metsss, metabolic syndrome severity score; aICAS, Asymptomatic Intracranial Arterial Stenosis.

Table S2: Univariate Logistic Regression Analysis for association with aICAS in the subset aged ≤ 65 years

Variables	OR (95%CI)	*P*
Male	0.92 (0.61 ~ 1.37)	0.665
Hypertension	2.64 (1.79 ~ 3.91)	<0.001
Diabetes mellitus	2.67 (1.62 ~ 4.40)	<0.001
Coronary heart disease	3.37 (1.56 ~ 7.32)	0.002
Dyslipidaemia	1.57 (0.88 ~ 2.80)	0.130
Smoking,	1.02 (0.67 ~ 1.54)	0.944
BMI, kg/m^2		
< 24.00	1.00 (Reference)	
24.00 -27.99	1.34 (0.84 ~ 2.14)	0.216
≥ 28.00	1.53 (0.90 ~ 2.59)	0.115
Hcy, per SD increase	1.01 (0.82 ~ 1.20)	0.887
Quartiles 0f hsCRP		
Q1 (< 0.33)	1.00 (Reference)	
Q2 (0.33-0.69)	1.07 (0.60 ~ 1.90)	0.815
Q3 (0.69-1.45)	0.97 (0.54 ~ 1.76)	0.928
Q4 (≥1.45)	1.78 (1.05 ~ 3.01)	0.032
MHR, per SD increase	1.11 (0.92 ~ 1.32)	0.264
NLR, per SD increase	1.09 (0.90 ~ 1.29)	0.334
LDL-C, per SD increase	1.05 (0.86 ~ 1.26)	0.644
TC, per SD increase	1.02 (0.84 ~ 1.23)	0.880
ApoA1, per SD increase	0.93 (0.76 ~ 1.13)	0.476
ApoB, per SD increase	1.07 (0.88 ~ 1.29)	0.501
Metabolic Syndrome	1.80 (1.21 ~ 2.66)	0.003
No. of MetS Component		
≤1	1.00 (Reference)	
2	1.48 (0.89 ~ 2.46)	0.130
3	2.03 (1.22 ~ 3.39)	0.006
≥4	2.21 (1.23 ~ 3.97)	0.008
Metsss, per SD increase	1.34 (1.13 ~ 1.59)	0.001

OR, odds ratio; CI, confidence interval; SD, standard deviation; BMI, body mass index; Hcy, homocysteine; hsCRP, high-sensitivity C-reactive protein; MHR, monocyte-to-high-density lipoprotein-cholesterol ratio; NLR, neutrophil-lymphocyte ratio; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; MetS, metabolic syndrome; Metsss, metabolic syndrome severity score; aICAS, asymptomatic intracranial arterial stenosis.

Table S3. Multivariate Logistic Regression Analysis for association with circulatory patterns of aICAS

Circulation, n (%)	Variables	Model1 * OR (95%CI)	P	Model2 † OR (95%CI)	P	Model3 ‡ OR (95%CI)	P
no aICAS		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
posterior	MetS	3.71 (2.04 ~ 6.76)	<0.001	3.02 (1.65 ~ 5.55)	<0.001	2.84 (1.54 ~ 5.23)	0.001
	Metsss	3.41 (1.90 ~ 6.12)	<0.001	3.13 (1.73 ~ 5.66)	<0.001	2.93 (1.61 ~ 5.33)	<0.001
anterior	MetS	1.43(0.90 ~ 2.27)	0.128	1.32(0.82 ~ 2.11)	0.254	1.26 (0.79 ~ 2.03)	0.336
	Metsss	1.34(0.82 ~ 2.18)	0.242	1.31 (0.80 ~ 2.15)	0.283	1.25 (0.76 ~ 2.06)	0.376
both	MetS	0.68 (0.14 ~ 3.29)	0.633	0.64 (0.13 ~ 3.16)	0.581	0.65 (0.13 ~ 3.23)	0.594
	Metsss	0.89 (0.19 ~ 4.31)	0.887	0.91 (0.19 ~ 4.43)	0.904	0.92 (0.19 ~ 4.57)	0.923

OR, odds ratio; CI, confidence interval; MetS, metabolic syndrome; Metsss, metabolic syndrome severity score; aICAS, asymptomatic intracranial arterial stenos; hsCRP, high-sensitivity C-reactive protein.

MetS: Using no MetS as the reference group; Metsss: Represents the fourth quartile of Metsss, using the first to third quartiles as the reference group.

* Model1: Unadjusted; † Model2: Adjusted for age, gender, coronary heart disease; ‡ Model3: Adjusted for Model2+ hsCRP.

Table S4: Interactive effects of hsCRP and MetS on risk of aICAS

Interactive items	Effect value	95%CI
Additive scale		
RERI	-0.05	-1.64~1.48
AP	-0.02	-0.92~0.39
S index	0.97	0.34~2.72
Multiplicative scale	0.82	0.39~1.75

RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S index, synergy index; CI, confidence interval; OR, odds ratio; MetS, metabolic syndrome; aICAS, asymptomatic intracranial arterial stenos; hsCRP, high-sensitivity C-reactive protein; MHR, monocyte-to-high-density lipoprotein-cholesterol ratio; NLR, neutrophil-lymphocyte ratio; Adjusted for age, sex, coronary heart disease, MHR, NLR.

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Table S5: Interactive effects of hsCRP and MetS on risk of aICAS in the subgroup aged ≤ 65 years

Interactive items	Effect value	95%CI
Additive scale		
RERI	0.20	-1.62~1.96
AP	0.08	-0.82~0.48
S index	1.14	0.38~3.41
Multiplicative scale	0.90	0.39~2.07

RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S index, synergy index; CI, confidence interval; MetS, metabolic syndrome; hsCRP, high-sensitivity C-reactive protein. Adjusted for sex and coronary heart disease.

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Table S6. Comparison of three preceding studies on the association between MetS and aICAS with our study

Characteristics	Kongcun Town study	APAC study	Shunyi study	Present study
Sample size	1988	5393	943	2390
Population	population-based	community-based	community-based	healthy check-up population
Age, year	57.6 (10.3)	55.2 (11.8)	55.6 (9.2)	52.0 (44.0, 58.0)
Male, n (%)	956 (48.0)	3230 (59.9)	340 (36.1)	1469 (61.5)
BMI, kg/m²	25.1 (3.3)	24.9 (3.3)	26.5 (3.7)	25.4 (23.2, 27.8)
MetS, n (%)	909 (45.7)	1323 (24.5)	496 (52.6)	726 (30.4)
aICAS, n (%)	132 (6.6)	713 (13.2)	123 (13.0)	135 (5.7)
aICAS detection method	MRA when TCD were positive	TCD	MRA	MRA

MetS, metabolic syndrome; aICAS, asymptomatic Intracranial Arterial Stenosis; BMI, body mass index; APAC, the Asymptomatic Polyvascular Abnormalities Community study.

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