Supplementary Materials

Inverse Association Between High-Density Lipoprotein Cholesterol and Adverse Outcomes Among Acute Ischemic Stroke Patients with Diabetes Mellitus

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Supplementary Tables

Supplementary Table S1 Characteristics of Patients Included According to HDL-C Quintiles

| Characteristics | Overall | HDL-C quintiles | | | | | P value |
		Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L	
Patients, n	3,824	757	712	792	780	783	
SBP, mean (SD)	152.53±22.18	151.65±21.87	150.05±22.10	153.00±20.92	152.72±22.32	154.99±23.39	<0.001
DBP, mean (SD)	87.59±13.00	87.52±12.65	87.41±12.88	87.68±13.06	87.47±12.72	87.84±13.66	0.969
Medical history, n (%)							
History of dyslipidemia	409 (10.70)	92 (12.15)	78 (10.96)	80 (10.10)	85 (10.90)	74 (9.45)	0.504
Heart failure	27 (0.71)	10 (1.32)	3 (0.42)	4 (0.51)	3 (0.38)	7 (0.89)	0.141
Medication history, n (%)							
Antihypertensive agents	1,944 (50.84)	394 (52.05)	335 (47.05)	418 (52.78)	383 (49.10)	414 (52.87)	0.093
NIHSS on admission, n (%)							0.634
0-5	2,677 (70.01)	529 (69.88)	504 (70.79)	563 (71.09)	543 (69.62)	538 (68.71)	
6-15	1,064 (27.82)	205 (27.08)	195 (27.39)	217 (27.40)	218 (27.95)	229 (29.25)	
>=16	83 (2.17)	23 (3.04)	13 (1.83)	12 (1.52)	19 (2.44)	16 (2.04)	
Medication at discharge, n (%)							
Antihypertensive agents	2,083 (54.63)	414 (54.98)	370 (52.11)	433 (54.67)	423 (54.37)	443 (56.79)	0.501

DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.

Supplementary Table S2 Hazard Ratios (95% CIs) for Risk of Adverse Outcomes According to Quintiles of HDL-C in Patients Included in This Study

Outcome	HDL-C quintiles, mmol/L					P for trend	Each 1-mmol/L increase in HDL-C
	Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
6 months							
Recurrent stroke							
Recurrent ischemic stroke							
Events, n (%)	75 (9.91)	66 (9.27)	64 (8.08)	61 (7.82)	60 (7.66)		
Incidence, per 1000 person-years	220.64	206.13	178.22	171.55	167.77		
Adjusted HR*	1.44 (1.02-2.03)	1.36 (0.95-1.94)	1.14 (0.80-1.63)	1.09 (0.76-1.56)	1.00	0.020	0.66 (0.44-0.98)
Adjusted HR†	1.54 (1.05-2.28)	1.46 (0.99-2.15)	1.20 (0.82-1.76)	1.06 (0.72-1.57)	1.00	0.010	0.56 (0.36-0.89)
Recurrent hemorrhagic stroke							
Events, n (%)	5 (0.66)	7 (0.98)	4 (0.51)	4 (0.51)	4 (0.51)		
Incidence, per 1000 person-years	13.76	20.37	10.50	10.64	10.64		
Adjusted HR*	1.17 (0.31-4.45)	1.76 (0.51-6.14)	0.92 (0.23-3.72)	0.95 (0.24-3.81)	1.00	0.557	1.20 (0.29-4.86)
Adjusted HR†	1.71 (0.33-8.74)	1.71 (0.33-8.92)	1.57 (0.32-7.64)	1.75 (0.35-8.66)	1.00	0.491	1.06 (0.24-4.71)
MACEs							
Cardiovascular death							
Events, n (%)	6 (0.79)	6 (0.84)	9 (1.14)	7 (0.90)	13 (1.66)		
Incidence, per 1000 person-years	16.43	17.41	23.59	18.58	34.48		
Adjusted HR*	0.52 (0.20-1.39)	0.57 (0.21-1.52)	0.74 (0.31-1.75)	0.58 (0.23-1.45)	1.00	0.179	2.19 (0.92-5.18)
Adjusted HR†	0.45 (0.11-1.87)	0.53 (0.13-2.20)	1.25 (0.44-3.53)	0.75 (0.24-2.39)	1.00	0.346	1.92 (0.57-6.45)
Non-fatal stroke							
Events, n (%)	40 (5.28)	30 (4.21)	22 (2.78)	25 (3.21)	28 (3.58)		
Incidence, per 1000 person-years	112.57	88.84	58.49	67.49	75.67		
Adjusted HR*	1.58 (0.97-2.59)	1.25 (0.74-2.11)	0.81 (0.46-1.42)	0.93 (0.54-1.59)	1.00	0.045	0.73 (0.40-1.33)

Outcome	HDL-C quintiles, mmol/L					P for trend	Each 1-mmol/L increase in HDL-C
	Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Adjusted HR†	1.60 (0.94-2.72)	1.27 (0.73-2.2)	0.80 (0.45-1.44)	0.90 (0.51-1.57)	1.00	0.055	0.72 (0.38-1.38)
Non-fatal MI							
Events, n (%)	3 (0.40)	1 (0.14)	4 (0.51)	1 (0.13)	0 (0.00)		
Incidence, per 1000 person-years	8.22	2.90	10.50	2.66	0		
Adjusted HR*	-	-	-	-	-	-	0.06 (0.01-0.89)
Adjusted HR†	-	-	-	-	-	-	0.07 (0.004-1.10)
12 months							
Recurrent stroke							
Recurrent ischemic stroke							
Events, n (%)	86 (11.36)	82 (11.52)	83 (10.48)	71 (9.10)	69 (8.81)		
Incidence, per 1000 person-years	129.26	131.16	117.71	101.68	98.40		
Adjusted HR*	1.44 (1.04-1.99)	1.47 (1.06-2.04)	1.29 (0.94-1.78)	1.10 (0.79-1.54)	1.00	0.007	0.66 (0.45-0.95)
Adjusted HR†	1.61 (1.12-2.31)	1.60 (1.12-2.29)	1.41 (1.00-2.00)	1.11 (0.77-1.59)	1.00	0.002	0.54 (0.35-0.81)
Recurrent hemorrhagic stroke							
Events, n (%)	8 (1.06)	9 (1.26)	5 (0.63)	6 (0.77)	7 (0.89)		
Incidence, per 1000 person-years	11.10	13.26	6.61	8.05	9.40		
Adjusted HR*	1.01 (0.36-2.83)	1.22 (0.45-3.33)	0.63 (0.20-1.99)	0.78 (0.26-2.33)	1.00	0.763	1.47 (0.48-4.47)
Adjusted HR†	1.30 (0.40-4.21)	1.15 (0.35-3.82)	0.95 (0.28-3.25)	1.12 (0.34-3.64)	1.00	0.627	1.32 (0.40-4.34)
MACEs							
Cardiovascular death							
Events, n (%)	8 (1.06)	7 (0.98)	13 (1.64)	8 (1.03)	19 (2.43)		
Incidence, per 1000 person-years	11.02	10.26	17.15	10.70	25.42		

Outcome	HDL-C quintiles, mmol/L					P for trend	Each 1-mmol/L increase in HDL-C
	Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Adjusted HR*	0.43 (0.19-1.00)	0.41 (0.17-0.99)	0.68 (0.33-1.38)	0.42 (0.18-0.97)	1.00	0.034	2.50 (1.22-5.12)
Adjusted HR†	0.40 (0.14-1.18)	0.33 (0.10-1.06)	0.89 (0.40-2.02)	0.43 (0.16-1.15)	1.00	0.086	2.30 (0.88-5.98)
Non-fatal stroke							
Events, n (%)	53 (7.00)	49 (6.88)	41 (5.18)	37 (4.74)	37 (4.73)		
Incidence, per 1000 person-years	76.25	74.57	55.56	50.92	51.07		
Adjusted HR*	1.59 (1.04-2.44)	1.56 (1.01-2.41)	1.15 (0.73-1.79)	1.04 (0.66-1.64)	1.00	0.009	0.69 (0.42-1.14)
Adjusted HR†	1.74 (1.10-2.76)	1.64 (1.04-2.60)	1.22 (0.77-1.95)	1.01 (0.63-1.64)	1.00	0.004	0.60 (0.35-1.04)
Non-fatal MI							
Events, n (%)	3 (0.40)	2 (0.28)	5 (0.63)	2 (0.26)	0 (0.00)		
Incidence, per 1000 person-years	4.14	2.93	6.62	2.68	0		
Adjusted HR*	-	-	-	-	-	-	0.13 (0.01-1.32)
Adjusted HR†	-	-	-	-	-	-	0.14 (0.01-1.69)

HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; MACEs, major adverse cardiovascular events; MI, myocardial infarction.

* model 1: age, sex

† model 2: age, sex, body mass index, smoking, drinking, hypertension, history of dyslipidemia, history of stroke, history of atrial fibrillation, history of coronary heart disease, medication history of antiplatelet agents, medication history of lipid-lowering drugs, low-density lipoprotein cholesterol, triglycerides, National Institutes of Health Stroke Scale on admission, TOAST, use of antiplatelet agents at discharge, use of anticoagulant agents at discharge, and use of statins at discharge.

Supplementary Table S3 Sensitivity Analysis for the Association between HDL-C and Adverse Outcomes

Outcomes	HDL-C quintiles, mmol/L					P for trend	Each 1-mmol/L increase in HDL-C
	Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
6 months							
Recurrent stroke							
Events, n (%)	75 (10.33)	64 (9.41)	62 (8.39)	59 (8.17)	56 (7.87)		
Incidence, per 1000 person-years	230.90	208.84	185.23	178.28	171.77		
Adjusted HR*	1.44 (1.01-2.05)	1.32 (0.92-1.90)	1.14 (0.79-1.64)	1.10 (0.76-1.58)	1.00	0.025	0.72 (0.47-1.08)
Adjusted HR†	1.50 (1.02-2.21)	1.33 (0.89-1.98)	1.16 (0.78-1.71)	1.03 (0.69-1.53)	1.00	0.022	0.66 (0.42-1.05)
MACEs							
Events, n (%)	78 (10.74)	67 (9.85)	68 (9.20)	62 (8.59)	58 (8.15)		
Incidence, per 1000 person-years	240.19	218.63	203.46	187.44	177.91		
Adjusted HR*	1.45 (1.03-2.05)	1.34 (0.94-1.91)	1.21 (0.85-1.72)	1.11 (0.78-1.60)	1.00	0.020	0.69 (0.46-1.04)
Adjusted HR†	1.52 (1.04-2.22)	1.36 (0.92-2.00)	1.24 (0.85-1.81)	1.03 (0.70-1.51)	1.00	0.014	0.63 (0.40-0.99)
12 months							
Recurrent stroke							
Events, n (%)	89 (12.26)	80 (11.76)	81 (10.96)	69 (9.56)	68 (9.55)		
Incidence, per 1000 person-years	140.29	133.89	123.47	105.93	106.31		
Adjusted HR*	1.42 (1.03-1.95)	1.37 (0.98-1.90)	1.23 (0.89-1.70)	1.05 (0.75-1.48)	1.00	0.012	0.73 (0.50-1.07)
Adjusted HR†	1.53 (1.07-2.17)	1.40 (0.98-2.00)	1.29 (0.92-1.83)	1.02 (0.71-1.47)	1.00	0.006	0.65 (0.43-0.98)
MACEs							

Outcomes	HDL-C quintiles, mmol/L					P for trend	Each 1-mmol/L increase in HDL-C
	Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Events, n (%)	92 (12.67)	84 (12.35)	88 (11.91)	73 (10.11)	72 (10.11)		
Incidence, per 1000 person-years	145.27	140.63	134.75	112.25	112.57		
Adjusted HR*	1.37 (1.00-1.88)	1.34 (0.98-1.85)	1.26 (0.92-1.72)	1.05 (0.76-1.46)	1.00	0.017	0.73 (0.51-1.06)
Adjusted HR†	1.46 (1.03-2.06)	1.36 (0.96-1.93)	1.32 (0.94-1.84)	1.00 (0.70-1.42)	1.00	0.009	0.65 (0.44-0.98)

HDL-C, high-density lipoprotein cholesterol; MACEs, major adverse cardiovascular events.

* model 1: age, sex

† model 2: age, sex, body mass index, smoking, drinking, hypertension, history of dyslipidemia, history of stroke, history of atrial fibrillation, history of coronary heart disease, medication history of antiplatelet agents, medication history of lipid-lowering drugs, low-density lipoprotein cholesterol, triglycerides, National Institutes of Health Stroke Scale on admission, TOAST, use of antiplatelet agents at discharge, use of anticoagulant agents at discharge, and use of statins at discharge.

Supplementary Table S4 Multivariable Analysis of Association between Low Levels of HDL-C and Adverse Outcomes within 1 year Compared with Normal Levels of HDL-C

	Events, n (%)	Model 1[*]: HR (95% CI)	P value	Model 2[†]: HR (95% CI)	P value
6 months					
Recurrent stroke	243 (9.52)	1.29 (1.02-1.63)	0.038	1.40 (1.07-1.82)	0.014
MACEs	259 (10.15)	1.33 (1.06-1.68)	0.016	1.45 (1.12-1.88)	0.005
12 months					
Recurrent stroke	299 (11.72)	1.34 (1.08-1.67)	0.008	1.47 (1.16-1.87)	0.002
MACEs	318 (12.46)	1.35 (1.09-1.67)	0.005	1.47 (1.17-1.86)	0.001

HDL-C, high-density lipoprotein cholesterol; MACEs, major adverse cardiovascular events.

* model 1: age, sex

† model 2: age, sex, body mass index, smoking, drinking, hypertension, history of dyslipidemia, history of stroke, history of atrial fibrillation, history of coronary heart disease, medication history of antiplatelet agents, medication history of lipid-lowering drugs, low-density lipoprotein cholesterol, triglycerides, National Institutes of Health Stroke Scale on admission, TOAST, use of antiplatelet agents at discharge, use of anticoagulant agents at discharge, and use of statins at discharge.

Supplementary Table S5.1 Subgroup Analysis for the Association between HDL-C and Recurrent Stroke at 6 Months

| Subgroup | Events (%) | HDL-C quintiles, mmol/L | | | | | P for trend | P for interaction |
		Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Age								
<65 years	171 (7.91)	1.43 (0.81-2.53)	1.40 (0.81-2.43)	1.20 (0.69-2.08)	1.06 (0.60-1.86)	1.00	0.131	0.960
≥65 years	173 (10.41)	1.80 (1.08-3.01)	1.63 (0.95-2.78)	1.18 (0.70-2.01)	1.12 (0.66-1.89)	1.00	0.015	
Sex								
Men	217 (8.62)	1.56 (0.94-2.59)	1.54 (0.93-2.55)	1.09 (0.64-1.85)	1.03 (0.60-1.77)	1.00	0.027	0.921
Women	127 (9.72)	1.52 (0.83-2.78)	1.33 (0.71-2.50)	1.43 (0.82-2.48)	1.15 (0.66-1.99)	1.00	0.133	
Smoking								
No	250 (9.32)	1.62 (1.05-2.50)	1.61 (1.04-2.47)	1.15 (0.74-1.77)	1.07 (0.69-1.65)	1.00	0.011	0.717
Yes	94 (8.22)	1.59 (0.71-3.53)	1.29 (0.57-2.90)	1.42 (0.65-3.10)	1.21 (0.54-2.72)	1.00	0.265	
Drinking								
No	287 (8.68)	1.44 (0.95-2.18)	1.43 (0.95-2.15)	1.10 (0.73-1.67)	1.08 (0.72-1.62)	1.00	0.044	0.923
Yes	57 (11.03)	2.68 (0.93-7.72)	2.27 (0.76-6.77)	2.15 (0.75-6.20)	1.24 (0.38-4.02)	1.00	0.036	
Hypertension								
No	21 (6.52)	0.22 (0.02-2.28)	1.28 (0.31-5.34)	0.69 (0.13-3.53)	0.99 (0.22-4.50)	1.00	0.420	0.517
Yes	323 (9.22)	1.71 (1.16-2.53)	1.53 (1.03-2.27)	1.25 (0.85-1.85)	1.13 (0.76-1.68)	1.00	0.003	
NIHSS score on admission								
0-4	147 (8.03)	2.19 (1.18-4.05)	1.85 (0.99-3.46)	1.64 (0.90-3.01)	1.74 (0.96-3.15)	1.00	0.017	0.325
≥4	197 (9.88)	1.31 (0.80-2.13)	1.35 (0.83-2.19)	1.01 (0.62-1.66)	0.83 (0.50-1.39)	1.00	0.118	
Ischemic stroke subtype								
Large-artery atherosclerosis	117 (11.05)	1.27 (0.63-2.55)	1.58 (0.81-3.07)	1.35 (0.70-2.63)	1.19 (0.60-2.37)	1.00	0.346	0.682
Cardiac	23 (10.85)	0.54 (0.12-2.53)	0.61 (0.10-3.60)	0.37 (0.07-1.82)	0.33 (0.07-1.50)	1.00	0.368	

embolism							
Small-vessel occlusion	51 (5.91)	2.01 (0.69-5.84)	3.27 (1.20-8.88)	1.51 (0.52-4.35)	1.21 (0.40-3.68)	1.00	0.052
Other	153 (9.05)	2.03 (1.17-3.54)	1.34 (0.73-2.45)	1.27 (0.71-2.26)	1.25 (0.71-2.19)	1.00	0.018

HDL-C, high-density lipoprotein cholesterol; NIHSS, National Institutes of Health Stroke Scale.

Supplementary Table S5.2 Subgroup Analysis for the Association between HDL-C and MACEs at 6 Months

Subgroup	Events (%)	HDL-C quintiles, mmol/L					P for trend	P for interaction
		Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Age								
<65 years	177 (8.19)	1.37 (0.78-2.38)	1.38 (0.81-2.35)	1.11 (0.65-1.89)	0.97 (0.56-1.69)	1.00	0.138	0.910
≥65 years	186 (11.19)	1.94 (1.17-3.21)	1.74 (1.03-2.95)	1.45 (0.88-2.40)	1.19 (0.71-1.98)	1.00	0.005	
Sex								
Men	231 (9.18)	1.57 (0.96-2.57)	1.53 (0.94-2.49)	1.14 (0.69-1.88)	0.95 (0.56-1.61)	1.00	0.014	0.851
Women	132 (10.10)	1.55 (0.85-2.83)	1.46 (0.79-2.69)	1.56 (0.91-2.67)	1.25 (0.73-2.13)	1.00	0.094	
Smoking								
No	263 (9.81)	1.66 (1.08-2.54)	1.72 (1.13-2.62)	1.20 (0.79-1.84)	1.09 (0.71-1.67)	1.00	0.005	0.505
Yes	100 (8.75)	1.55 (0.72-3.31)	1.15 (0.53-2.54)	1.46 (0.70-3.06)	1.08 (0.49-2.37)	1.00	0.253	
Drinking								
No	306 (9.25)	1.49 (0.99-2.22)	1.48 (0.99-2.21)	1.19 (0.80-1.77)	1.07 (0.72-1.59)	1.00	0.021	0.952
Yes	57 (11.03)	2.68 (0.93-7.72)	2.27 (0.76-6.77)	2.15 (0.75-6.20)	1.24 (0.38-4.02)	1.00	0.036	
Hypertension								
No	22 (6.83)	0.44 (0.07-2.88)	1.27 (0.31-5.18)	0.63 (0.13-3.19)	0.93 (0.20-4.23)	1.00	0.611	0.686
Yes	341 (9.74)	1.72 (1.17-2.51)	1.57 (1.07-2.31)	1.33 (0.91-1.94)	1.12 (0.76-1.65)	1.00	0.002	
NIHSS score on admission								
0-4	152 (8.30)	1.97 (1.09-3.56)	1.67 (0.91-3.05)	1.44 (0.80-2.60)	1.54 (0.87-2.74)	1.00	0.032	0.491
≥4	211 (10.59)	1.45 (0.90-2.34)	1.48 (0.92-2.38)	1.22 (0.76-1.95)	0.86 (0.52-1.43)	1.00	0.035	
Ischemic stroke subtype								
Large-artery atherosclerosis	125 (11.80)	1.23 (0.62-2.44)	1.62 (0.85-3.09)	1.49 (0.79-2.82)	1.26 (0.65-2.43)	1.00	0.376	0.460
Cardiac	23 (10.85)	0.54 (0.12-2.53)	0.61 (0.10-3.60)	0.37 (0.07-1.82)	0.33 (0.07-1.50)	1.00	0.368	

embolism							
Small-vessel occlusion	54 (6.26)	1.97 (0.68-5.73)	3.66 (1.37-9.76)	1.66 (0.59-4.68)	1.21 (0.40-3.67)	1.00	0.040
Other	161 (9.53)	2.17 (1.27-3.70)	1.33 (0.74-2.42)	1.31 (0.75-2.29)	1.18 (0.67-2.05)	1.00	0.006

HDL-C, high-density lipoprotein cholesterol; MACEs, major adverse cardiovascular events; NIHSS, National Institutes of Health Stroke Scale.

Supplementary Table S5.3 Subgroup Analysis for the Association between HDL-C and Recurrent Stroke at 12 Months

Subgroup	Events (%)	HDL-C quintiles, mmol/L					P for trend	P for interaction
		Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Age								
<65 years	206 (9.53)	1.50 (0.89-2.53)	1.50 (0.91-2.48)	1.25 (0.76-2.07)	1.18 (0.71-1.95)	1.00	0.077	0.948
≥65 years	212 (12.76)	1.72 (1.08-2.75)	1.64 (1.01-2.65)	1.37 (0.87-2.18)	1.05 (0.65-1.69)	1.00	0.008	
Sex								
Men	267 (10.61)	1.58 (1.01-2.49)	1.56 (1.00-2.45)	1.13 (0.71-1.81)	1.10 (0.68-1.76)	1.00	0.014	0.618
Women	151 (11.55)	1.56 (0.89-2.74)	1.44 (0.81-2.57)	1.69 (1.03-2.77)	1.08 (0.64-1.82)	1.00	0.052	
Smoking								
No	307 (11.45)	1.55 (1.04-2.30)	1.55 (1.05-2.29)	1.30 (0.89-1.89)	1.06 (0.71-1.56)	1.00	0.008	0.970
Yes	111 (9.71)	1.99 (0.93-4.25)	1.77 (0.83-3.78)	1.59 (0.74-3.42)	1.47 (0.68-3.20)	1.00	0.069	
Drinking								
No	354 (10.70)	1.52 (1.05-2.22)	1.48 (1.02-2.15)	1.26 (0.87-1.82)	1.13 (0.79-1.64)	1.00	0.012	0.899
Yes	64 (12.38)	2.30 (0.86-6.12)	2.39 (0.91-6.26)	2.04 (0.79-5.24)	0.99 (0.33-3.01)	1.00	0.032	
Hypertension								
No	25 (7.76)	0.18 (0.02-1.91)	1.75 (0.47-6.57)	0.56 (0.11-2.85)	1.18 (0.29-4.90)	1.00	0.464	0.232
Yes	393 (11.22)	1.73 (1.21-2.46)	1.54 (1.08-2.20)	1.38 (0.98-1.96)	1.13 (0.79-1.62)	1.00	<0.001	
NIHSS score on admission								
0-4	181 (9.89)	1.98 (1.14-3.41)	1.88 (1.09-3.24)	1.71 (1.01-2.89)	1.43 (0.83-2.44)	1.00	0.008	0.561
≥4	237 (11.89)	1.39 (0.89-2.19)	1.39 (0.89-2.18)	1.13 (0.72-1.77)	0.98 (0.62-1.56)	1.00	0.070	
Ischemic stroke subtype								
Large-artery atherosclerosis	140 (13.22)	1.37 (0.73-2.59)	1.78 (0.97-3.24)	1.51 (0.83-2.76)	1.25 (0.67-2.33)	1.00	0.175	0.640
Cardiac	29 (13.68)	0.87 (0.23-3.30)	0.53 (0.09-3.06)	0.79 (0.21-2.89)	0.29 (0.07-1.30)	1.00	0.866	

embolism							
Small-vessel occlusion	69 (8.00)	1.08 (0.45-2.63)	1.95 (0.88-4.30)	1.07 (0.47-2.45)	1.06 (0.46-2.44)	1.00	0.433
Other	180 (10.65)	2.23 (1.33-3.74)	1.55 (0.89-2.70)	1.44 (0.85-2.45)	1.25 (0.74-2.13)	1.00	0.002

HDL-C, high-density lipoprotein cholesterol; NIHSS, National Institutes of Health Stroke Scale.

Supplementary Table S5.4 Subgroup Analysis for the Association between HDL-C and MACEs at 12 Months

Subgroup	Events (%)	HDL-C quintiles, mmol/L					P for trend	P for interaction
		Q1, <0.71 mmol/L	Q2, 0.71-0.83 mmol/L	Q3, 0.83-0.95 mmol/L	Q4, 0.95-1.11 mmol/L	Q5, ≥1.11 mmol/L		
Age								
<65 years	217 (10.04)	1.32 (0.80-2.19)	1.40 (0.87-2.25)	1.14 (0.71-1.84)	1.01 (0.62-1.66)	1.00	0.132	0.830
≥65 years	226 (13.60)	1.79 (1.13-2.83)	1.69 (1.05-2.71)	1.57 (1.01-2.45)	1.12 (0.70-1.79)	1.00	0.004	
Sex								
Men	288 (11.44)	1.48 (0.96-2.28)	1.48 (0.97-2.26)	1.16 (0.75-1.79)	0.98 (0.62-1.54)	1.00	0.017	0.687
Women	155 (11.86)	1.58 (0.90-2.77)	1.54 (0.87-2.72)	1.74 (1.06-2.84)	1.16 (0.69-1.93)	1.00	0.041	
Smoking								
No	324 (12.09)	1.52 (1.03-2.24)	1.61 (1.10-2.35)	1.31 (0.91-1.90)	1.06 (0.72-1.55)	1.00	0.007	0.915
Yes	119 (10.41)	1.71 (0.84-3.47)	1.42 (0.69-2.91)	1.55 (0.77-3.12)	1.19 (0.57-2.49)	1.00	0.113	
Drinking								
No	378 (11.43)	1.47 (1.02-2.11)	1.47 (1.02-2.10)	1.29 (0.91-1.83)	1.09 (0.76-1.56)	1.00	0.013	0.888
Yes	65 (12.57)	2.22 (0.83-5.90)	2.29 (0.88-5.99)	2.15 (0.85-5.46)	0.98 (0.33-2.96)	1.00	0.038	
Hypertension								
No	26 (8.07)	0.37 (0.06-2.37)	1.73 (0.47-6.39)	0.54 (0.11-2.66)	1.13 (0.27-4.66)	1.00	0.627	0.326
Yes	417 (11.91)	1.63 (1.16-2.30)	1.52 (1.07-2.15)	1.41 (1.01-1.97)	1.09 (0.77-1.54)	1.00	0.001	
NIHSS score on admission								
0-4	188 (10.27)	1.74 (1.03-2.95)	1.67 (0.99-2.82)	1.49 (0.90-2.47)	1.30 (0.78-2.17)	1.00	0.024	0.809
≥4	255 (12.79)	1.44 (0.92-2.23)	1.46 (0.94-2.26)	1.31 (0.86-2.01)	0.97 (0.62-1.52)	1.00	0.034	
Ischemic stroke subtype								
Large-artery	150 (14.16)	1.33 (0.71-2.48)	1.84 (1.02-3.30)	1.68 (0.94-2.99)	1.29 (0.71-2.37)	1.00	0.183	0.366

atherosclerosis							
Cardiac embolism	31 (14.62)	0.76 (0.20-2.80)	0.37 (0.06-2.16)	0.77 (0.22-2.67)	0.31 (0.08-1.24)	1.00	0.687
Small-vessel occlusion	72 (8.34)	1.07 (0.44-2.59)	2.15 (0.99-4.68)	1.15 (0.51-2.59)	1.05 (0.46-2.43)	1.00	0.365
Other	190 (11.24)	2.10 (1.29-3.44)	1.39 (0.81-2.37)	1.34 (0.80-2.23)	1.09 (0.65-1.82)	1.00	0.002

HDL-C, high-density lipoprotein cholesterol; MACEs, major adverse cardiovascular events; NIHSS, National Institutes of Health Stroke Scale.

Supplementary Figure

Acute ischemic stroke or TIA patients in CNSR-III
(N=15,166)

Not included in biomarker subgroup (N=3,905)

Patients having blood sample (N=11,261)

Patients with TIA (N=899)
Patients without diabetes mellitus (N=6,294)
Patients with missing data of HDL-C (N=244)

Patients with acute ischemic stroke, diabetes mellitus
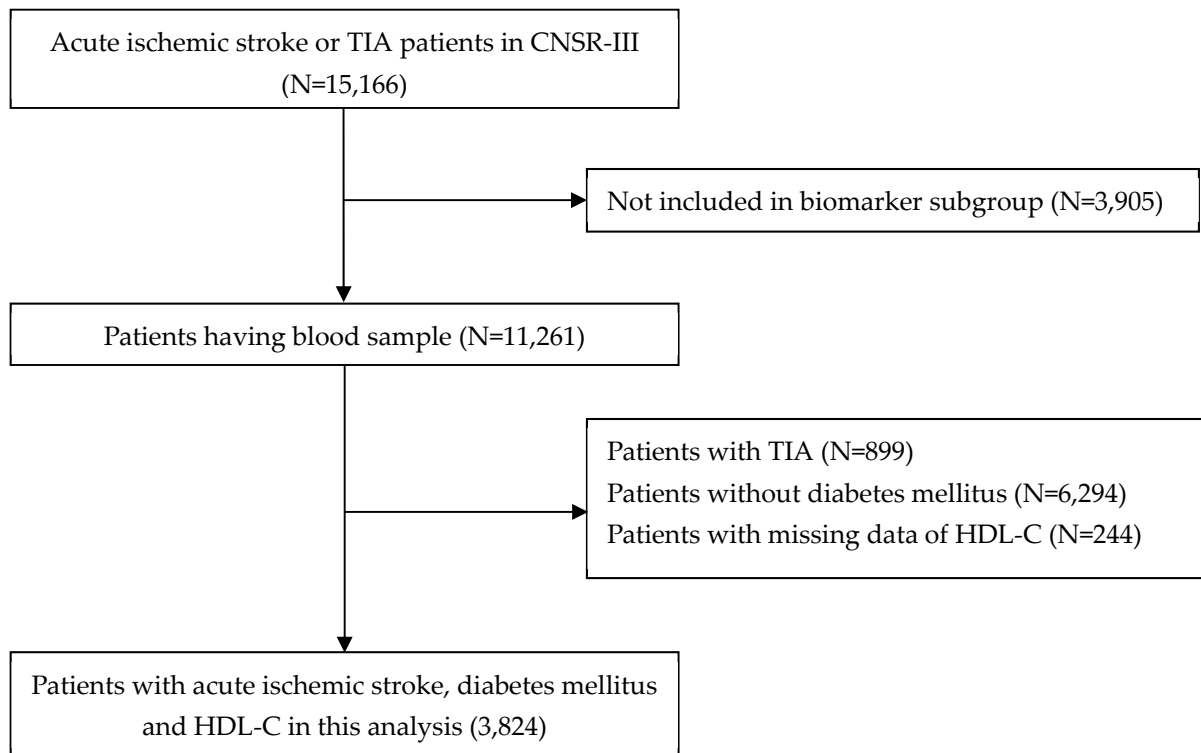and HDL-C in this analysis (3,824)

Figure S1 Flow Chart of the Study Population

TIA, transient ischemic attack; CNSR-III, Third China National Stroke Registry; HDL-C, high-density lipoprotein cholesterol