

SUPPLEMENTAL MATERIAL

Table S1. Comparison of baseline characteristics of participants and nonparticipants

Characteristics	Nonparticipants	Participants	<i>P</i> value
n	9531	5635	
Age, y	63.0(54.0-71.0)	62.0(54.0-70.0)	0.0048
Men, n (%)	3808(67.58)	6556(68.79)	0.1221
BMI, kg/m ²	24.24(22.49-26.29)	24.51(22.67-26.67)	<0.0001
Medical History, n (%)			
Hypertension	3536(62.75)	5958(62.51)	0.7689
Diabetes mellitus	1267(22.48)	2243(23.53)	0.1387
Dyslipidemia	390(6.92)	801(8.40)	0.0010
Stroke or TIA	1165(20.67)	2190(22.98)	0.0010
Atrial fibrillation/flutter	398(7.06)	621(6.52)	0.1932
Peripheral vascular disease	52(0.92)	66(0.69)	0.1188
Heart failure	30(3.77)	64(4.81)	0.2589
COPD	51(0.91)	81(0.85)	0.7236
Stroke type/Subtype, n (%)			
Ischemic stroke	5314(94.30)	8832(92.67)	0.0001
TIA	321(5.70)	699(7.33)	
TOAST, n (%)			
Large-artery atherosclerosis	1456(25.84)	2400(25.18)	0.0167
Cardioembolism	373(6.62)	544(5.71)	
Small-vessel occlusion	1199(21.28)	1966(20.63)	
Other determined etiology	56(0.99)	126(1.32)	
Undetermined etiology	2551(45.27)	4495(47.16)	
Current smoker, n (%)	1663(29.51)	3089(32.41)	0.0005
Medication in hospital, n (%)			

Cholesterol-lowering agents	5324(95.31)	9182(96.99)	<0.0001
Antihypertensive agents	2432(43.54)	4568(48.25)	<0.0001
Hypoglycemic agents	1343(24.04)	2449(25.87)	0.0126
Antiplatelet agents	5422(97.06)	9191(97.08)	0.9424
Anticoagulant agents	697(12.48)	849(8.97)	<0.0001
NIHSS score on admission	3(1-6)	3(1-6)	0.0010
Time from onset of symptoms to admission, h	13.00 (3.00-41.00)	15.00(3.00-45.00)	0.0213
Lipid level			
TC, mmol/L	3.97(3.31-4.69)	3.97(3.31-4.74)	0.7080
LDL, mmol/L	2.32(1.75-2.98)	2.30(1.71-2.97)	0.2338
HDL, mmol/L	0.94(0.78-1.13)	0.93(0.77-1.11)	0.0060
TG, mmol/L	1.35(1.02-1.85)	1.38(1.04-1.89)	0.0385
FBG, mmol/L	5.48(4.87-6.74)	5.56(4.90-6.99)	0.0028
eGFR, mL/min/1.73 m ²	92.73(81.15-101.75)	93.31(81.94-102.03)	0.1256
hs-CRP, mg/L	1.77(0.83-4.75)	1.78(0.81-4.71)	0.9442
Medication on discharge, n (%)			
Cholesterol-lowering agents	5080(90.33)	8571(92.06)	0.0003
Antihypertensive agents	2578(45.84)	4840(50.91)	<0.0001
Hypoglycemic agents	1248(22.19)	2298(24.17)	0.0054
Antiplatelet agents	5034(89.67)	8668(91.17)	0.0021
Anticoagulant agents	189(3.36)	260(2.73)	0.0284

Abbreviations: BMI=body mass index; COPD= chronic obstructive pulmonary disease; TIA=transient Ischemic Attack; TOAST= Trial of Org 10172 in Acute Stroke Treatment, NIHSS=The National Institutes of Health Stroke Scale; TC=total cholesterol; LDL=low-density lipoprotein cholesterol; HDL=high-density lipoprotein cholesterol; TG=triglycerides; FBG=fasting blood glucose; eGFR=estimated glomerular filtration rate; hs-CRP=high sensitivity C-reactive protein. Continuous variables are expressed as median with interquartile range. Categorical variables are expressed as frequency with percentage.

Table S2. Subgroup analyses for the associations of CO₂CP with all-cause death and poor functional outcomes.

Outcomes	Quintiles of CO ₂ CP, mmol/L					<i>P</i> _{interaction}
	Q1	Q2	Q3	Q4	Q5	
Age						
At 3 months						
Age<65 years						
Death	0.81(0.26-2.49)	0.48(0.15-1.52)	0.38(0.10-1.38)	Reference	1.21(0.41-3.58)	0.1507
mRS score 3-6	1.36(0.97-1.91)	1.16(0.83-1.62)	1.05(0.75-1.47)	Reference	1.02(0.72-1.44)	0.7900
mRS score 2-6	1.20(0.93-1.55)	1.11(0.87-1.42)	0.97(0.76-1.24)	Reference	1.11(0.86-1.42)	0.5358
Age≥ 65 years						
Death	4.53(1.87-10.96)	2.49(1.00-6.18)	2.13(0.84-5.40)	Reference	1.61(0.63-4.12)	
mRS score 3-6	1.65(1.20-2.27)	1.32(0.96-1.80)	1.38(1.00-1.90)	Reference	0.96(0.70-1.33)	
mRS score 2-6	1.26(0.97-1.63)	1.04(0.80-1.33)	1.15(0.89-1.48)	Reference	0.95(0.74-1.22)	
At 1 year						
Age<65 years						
Death	0.91(0.41-2.03)	0.62(0.28-1.42)	1.06(0.50-2.26)	Reference	1.27(0.60-2.69)	0.0937

mRS score 3-6	1.38(0.96-1.98)	1.08(0.75-1.55)	1.12(0.79-1.60)	Reference	1.22(0.85-1.76)	0.5234
mRS score 2-6	1.33(1.02-1.73)	1.12(0.87-1.44)	1.16(0.91-1.49)	Reference	1.12(0.87-1.45)	0.8738
Age ≥ 65 years						
Death	1.88(1.42-2.53)	1.46(1.10-1.94)	1.42(1.06-1.89)	Reference	1.02(0.77-1.37)	
mRS score 3-6	1.24(0.91-1.68)	0.94(0.69-1.27)	1.08(0.79-1.46)	Reference	0.88(0.65-1.19)	
mRS score 2-6	1.33(1.02-1.72)	1.14(0.89-1.46)	1.12(0.87-1.45)	Reference	0.98(0.77-1.27)	
Gender						
At 3 months						
Male						
Death	2.11(0.85-5.23)	2.53(1.03-6.16)	1.22(0.47-3.18)	Reference	1.95(0.77-4.89)	0.4843
mRS score 3-6	1.42(1.07-1.89)	1.24(0.93-1.65)	1.33(1.01-1.76)	Reference	0.94(0.70-1.26)	0.4217
mRS score 2-6	1.16(0.93-1.45)	1.05(0.85-1.31)	1.02(0.82-1.26)	Reference	1.04(0.84-1.29)	0.9366
Female						
Death	2.68(1.03-6.96)	1.19(0.62-2.28)	1.46(0.77-2.78)	Reference	0.59(0.27-1.29)	

mRS score 3-6	2.12(1.43-3.14)	1.38(0.94-2.02)	1.10(0.73-1.65)	Reference	1.08(0.72-1.60)	
mRS score 2-6	1.62(1.17-2.23)	1.23(0.91-1.67)	1.27(0.93-1.75)	Reference	1.06(0.76-1.46)	
At 1 year						
Male						
Death	1.31(0.75-2.28)	1.53(0.89-2.64)	1.28(0.74-2.22)	Reference	1.47(0.85-2.55)	0.2021
mRS score 3-6	1.28(0.96-1.70)	1.09(0.82-1.46)	1.14(0.86-1.51)	Reference	1.07(0.80-1.44)	0.8290
mRS score 2-6	1.27(1.02-1.59)	1.15(0.92-1.43)	1.10(0.89-1.36)	Reference	1.09(0.88-1.36)	0.8300
Female						
Death	2.12(1.07-4.17)	1.24(0.62-2.49)	1.53(0.77-3.03)	Reference	0.60(0.26-1.36)	
mRS score 3-6	1.46(0.99-2.16)	0.95(0.65-1.39)	1.09(0.74-1.61)	Reference	0.89(0.60-1.32)	
mRS score 2-6	1.61(1.17-2.22)	1.20(0.89-1.63)	1.38(1.01-1.90)	Reference	1.02(0.74-1.40)	
Stroke subtypes						
At 3 months						
Ischemic stroke						

Death	2.38(1.26-4.51)	1.57(0.82-3.01)	1.16(0.58-2.31)	Reference	1.28(0.64-2.54)	0.7622
mRS score 3-6	1.56(1.24-1.97)	1.26(1.00-1.58)	1.24(0.98-1.56)	Reference	0.95(0.75-1.20)	0.7137
mRS score 2-6	1.23(1.03-1.48)	1.08(0.91-1.29)	1.07(0.89-1.27)	Reference	1.01(0.85-1.21)	0.8722
TIA						
Death				Reference		
mRS score 3-6	0.98(0.06-16.29)	1.35(0.12-15.39)	1.66(0.16-17.75)	Reference	0.98(0.08-11.71)	
mRS score 2-6	2.52(0.57-11.09)	1.85(0.45-7.67)	2.13(0.55-8.30)	Reference	1.50(0.37-6.03)	
At 1 year						
Ischemic stroke						
Death	1.56(1.02-2.38)	1.33(0.87-2.03)	1.32(0.86-2.01)	Reference	1.05(0.68-1.65)	0.9907
mRS score 3-6	1.34(1.07-1.69)	0.99(0.79-1.25)	1.11(0.88-1.40)	Reference	0.98(0.78-1.23)	0.2221
mRS score 2-6	1.35(1.12-1.62)	1.13(0.95-1.36)	1.16(0.97-1.38)	Reference	1.07(0.89-1.28)	0.8889
TIA						
Death	7.63(0.02-3626.6)	1.38(0.02-84.45)	30.49	Reference	2.19(0.01-610)	

mRS score 3-6	0.62(0.06-6.61)	1.55(0.23-10.46)	1.61(0.20-12.97)	Reference	1.01(0.11-9.03)	
mRS score 2-6	1.57(0.44-5.60)	1.09(0.34-3.46)	2.35(0.77-7.19)	Reference	0.75(0.24-2.36)	
Smoking						
Current smoking						
Death	1.69(0.30-9.54)	3.34(0.71-15.67)	0.99(0.18-5.57)	Reference	1.54(0.30-7.82)	0.1856
mRS score 3-6	1.83(1.17-2.85)	1.54(0.98-2.44)	1.51(0.97-2.36)	Reference	1.38(0.87-2.21)	0.7411
mRS score 2-6	1.39(1.00-1.93)	1.13(0.80-1.58)	1.02(0.74-1.42)	Reference	1.28(0.91-1.80)	0.9321
No smoking						
Death	2.59 (1.28-5.23)	1.31(0.62-2.79)	1.03(0.47-2.25)	Reference	1.15(0.53-2.52)	
mRS score 3-6	1.60(1.22-2.10)	1.23(0.94-1.60)	1.19(0.91-1.56)	Reference	0.91(0.69-1.20)	
mRS score 2-6	1.25(1.01-1.56)	1.10(0.89-1.35)	1.08(0.88-1.34)	Reference	0.96(0.76-1.18)	
At 1 year						
Current smoking						
Death	2.17(0.77-6.11)	2.44(0.86-6.93)	2.03(0.73-5.68)	Reference	1.87(0.63-5.56)	0.8225

mRS score 3-6	1.47(0.95-2.28)	0.99(0.62-1.58)	1.27(0.81-1.97)	Reference	1.07(0.67-1.72)	0.6878
mRS score 2-6	1.56(1.12-2.18)	1.24(0.88-1.75)	1.33(0.96-1.85)	Reference	1.36(0.96-1.91)	0.4133
No smoking						
Death	1.38(0.87-2.21)	1.17(0.74-1.86)	1.16(0.73-1.84)	Reference	0.88(0.53-1.44)	
mRS score 3-6	1.28(0.97-1.68)	1.02(0.79-1.33)	1.07(0.82-1.40)	Reference	0.97(0.74-1.26)	
mRS score 2-6	1.30(1.04-1.61)	1.13(0.92-1.38)	1.11(0.90-1.37)	Reference	0.96(0.78-1.19)	
NIHSS						
At 3 months						
NIHSS<4						
Death	3.87(1.40-10.68)	1.61(0.54-4.77)	1.30(0.41-4.18)	Reference	0.92(0.29-2.86)	0.4801
mRS score 3-6	1.45(1.01-2.10)	1.04(0.72-1.49)	1.10(0.76-1.58)	Reference	0.78(0.54-1.14)	0.4643
mRS score 2-6	1.11(0.86-1.44)	0.98(0.77-1.24)	0.93(0.73-1.18)	Reference	0.93(0.73-1.18)	0.1799
NIHSS ≥ 4						
Death	1.36(0.56-3.26)	1.42(0.60-3.37)	1.03(0.41-2.59)	Reference	1.54(0.62-3.83)	

mRS score 3-6	1.61(1.20-2.17)	1.37(1.02-1.84)	1.48(1.10-1.99)	Reference	1.10(0.81-1.50)	
mRS score 2-6	1.42(1.09-1.85)	1.18(0.91-1.53)	1.33(1.03-1.73)	Reference	1.09(0.84-1.43)	
At 1 year						
NIHSS<4						
Death	2.12(1.11-4.04)	1.50(0.80-2.85)	1.35(0.69-2.64)	Reference	0.88(0.43-1.78)	0.3072
mRS score 3-6	1.29(0.91-1.84)	0.95(0.67-1.35)	1.08(0.77-1.53)	Reference	0.94(0.66-1.33)	0.9444
mRS score 2-6	1.43(1.11-1.84)	1.21(0.96-1.54)	1.13(0.89-1.44)	Reference	1.06(0.83-1.35)	0.3117
NIHSS ≥ 4						
Death	1.14(0.65-2.01)	1.05(0.60-1.86)	1.23(0.70-2.15)	Reference	1.26(0.71-2.26)	
mRS score 3-6	1.35(0.99-1.84)	1.01(0.74-1.39)	1.21(0.88-1.65)	Reference	1.04(0.76-1.44)	
mRS score 2-6	1.36(1.03-1.77)	1.04(0.80-1.36)	1.30(0.99-1.69)	Reference	1.06(0.81-1.39)	

Abbreviations: CO₂CP=carbon dioxide combining power; mRS=modified Rankin Scale; NIHSS=The National Institutes of Health Stroke Scale; TIA=transient ischemic attack

Adjusted for age, gender, body mass index, history of dyslipidemia, stroke or transient ischemic stroke, atrial fibrillation/flutter, stroke type, current smoke, antihypertensive agents, anticoagulant agents, NIHSS, high-density lipoprotein cholesterol, history of COPD, time from onset of symptoms to admission, and high sensitivity C-reactive protein on admission.

Table S3. Comparison of baseline characteristics of patients stratified by CO₂CP levels.

Characteristics	CO ₂ CP levels			P value
	<23 mmol/L	23-29 mmol/L	≥29 mmol/L	
n				
Age, y	62(53-70)	62(54-70)	63.5(55-70)	0.0122
Men, n (%)	1832(69.53)	4109(68.64)	615(67.58)	0.5112
BMI, kg/m ²	24.62(22.86-26.70)	24.49(22.66-26.64)	24.61(22.58-26.73)	0.2998
Medical History, n (%)				
Hypertension	1632(61.94)	3751(62.66)	575(63.19)	0.7276
Diabetes mellitus	590(22.39)	1440(24.06)	213(23.41)	0.2431
Dyslipidemia	187(7.10)	549(9.17)	65(7.14)	0.0021
Stroke or TIA	567(21.52)	1388(23.19)	235(25.82)	0.0237
Atrial fibrillation/flutter	197(7.48)	381(6.36)	43(4.73)	0.0111
Peripheral vascular disease	18(0.68)	40(0.67)	8(0.88)	0.7728
Heart failure	34(4.14)	21(5.72)	9(6.29)	0.3401
COPD	22 (0.83)	49 (0.82)	10(1.10)	0.6886
Stroke type/Subtype, n (%)				
Ischemic stroke	5527(92.33)	2469(93.70)	836(91.87)	0.0503
TIA	459(7.67)	166(6.30)	74(8.13)	

TOAST, n (%)				
Large-artery atherosclerosis	1486(24.82)	687(26.07)	227(24.95)	0.2416
Cardioembolism	336(5.61)	165(6.26)	43(4.73)	
Small-vessel occlusion	1269(21.20)	499(18.94)	198(21.76)	
Other determined etiology	80(1.34)	37(1.40)	9(0.99)	
Undetermined etiology	2815(47.03)	1247(46.32)	433(47.58)	
Current smoker, n (%)	1895(31.66)	921(34.95)	273(30.00)	0.0006
Medication in hospital, n (%)				
Cholesterol-lowering agents	5768(96.99)	2538(96.98)	876(97.01)	0.9990
Antihypertensive agents	2823(48.25)	1320(50.44)	425(47.07)	0.0305
Hypoglycemic agents	1559(26.21)	661(25.26)	229(25.36)	0.6057
Antiplatelet agents	5767(96.97)	2552(97.52)	872(96.57)	0.2420
Anticoagulant agents	491(8.26)	291(11.12)	67(7.42)	<0.0001
NIHSS score on admission	3(1-6)	3(1-6)	3(1-5)	<0.0001
Time from onset of symptoms to admission, h	13.00 (3.00-34.00)	15.00(3.00-46.00)	18.00(4.00-48.00)	0.0009
Lipid level				
TC, mmol/L	3.98(3.32-4.73)	3.94(3.31-4.75)	3.97(3.31-4.77)	0.8104
LDL, mmol/L	2.32(1.71-2.97)	2.27(1.70-2.97)	2.27(1.70-2.97)	0.5744

HDL, mmol/L	0.93(0.77-1.11)	0.91(0.77-1.12)	0.95(0.79-1.09)	0.0504
TG, mmol/L	1.39(1.06-1.91)	1.38(1.03-1.89)	1.37(1.05-1.86)	0.7563
FBG, mmol/L	5.58(4.89-6.95)	5.56(4.90-6.97)	5.52(4.90-7.10)	0.9095
eGFR, mL/min/1.73 m ²	92.83(80.74-102.55)	93.72(82.37-101.96)	92.83(82.72-101.01)	0.3129
hs-CRP, mg/L	1.97(0.87-5.47)	1.72(0.80-4.53)	1.62(0.79-4.21)	0.0011
Medication on discharge, n (%)				
Cholesterol-lowering agents	2440 (93.99)	5472(91.60)	839(92.30)	0.0861
Antihypertensive agents	1387(52.86)	3003(50.27)	450(49.50)	0.0582
Hypoglycemic agents	637(24.48)	1446(24.20)	215(23.65)	0.9264
Antiplatelet agents	2400(91.46)	5434(90.96)	834(91.75)	0.6113
Anticoagulant agents	86(3.28)	151(2.53)	23(2.53)	0.1345

Abbreviations: BMI=body mass index; CO₂CP=carbon dioxide combining power; COPD= chronic obstructive pulmonary disease; TIA=transient Ischemic Attack; TOAST=Trial of Org 10172 in Acute Stroke Treatment; NIHSS=The National Institutes of Health Stroke Scale; TC=total cholesterol; LDL=low-density lipoprotein cholesterol; HDL=high-density lipoprotein cholesterol; TG=triglycerides; FBG=fasting blood glucose; eGFR=estimated glomerular filtration rate; hs-CRP=high sensitivity C-reactive protein. Continuous variables are expressed as median with interquartile range. Categorical variables are expressed as frequency with percentage.

Table S4. Reclassification and discrimination statistics for outcomes at 3 months and 1 year by CO₂CP

	C statistics		IDI		NRI (continuous)		NRI (categorical) ^a	
	Estimate (95% CI)	<i>P</i> value	Estimate (95% CI), %	<i>P</i> value	Estimate (95% CI), %	<i>P</i> value	Estimate (95% CI), %	<i>P</i> value
Outcomes at 3 months								
Death								
Conventional model ^b	0.841 (0.805-0.876)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.843 (0.807-0.878)	0.6886	0.50 (0.06-0.94)	0.0254	19.43 (1.91-36.95)	0.0303	2.34 (-1.76-6.43)	0.2657
mRS score 3-6								
Conventional model ^b	0.809 (0.796-0.822)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.810 (0.797-0.823)	0.3550	0.20 (0.07-0.34)	0.0024	10.72 (4.86-16.58)	0.0003	0.02 (-1.59-1.23)	0.8004
mRS score 2-6								
Conventional model ^b	0.783 (0.773-0.795)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.784 (0.774-0.795)	0.7612	0.03 (-0.01-0.01)	0.1497	4.82 (0.25-9.39)	0.0388	0.01 (-0.1-0.05)	0.6700
Outcomes at 1 year								
Death								
Conventional model ^b	0.795 (0.768-0.823)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.798 (0.770-0.825)	0.3269	0.18 (-0.01-0.41)	0.1431	11.80 (-0.01-23.67)	0.0518	1.03 (-0.13-3.35)	0.3868
mRS score 3-6								

Conventional model ^b	0.799 (0.786-0.813)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.801 (0.787-0.814)	0.1937	0.11 (0.01-0.23)	0.0353	6.49 (0.51-12.46)	0.0334	0.18 (-1.05-1.40)	0.7790
mRS score 2-6								
Conventional model ^b	0.761 (0.750-0.772)		Reference		Reference		Reference	
Conventional model + CO ₂ CP	0.762 (0.751-0.773)	0.1822	0.07 (0.01-0.14)	0.0383	4.74 (0.04-9.43)	0.0483	0.03 (-0.12-0.06)	0.5369

Abbreviations: CI=confidence interval; CO₂CP=carbon dioxide combining power; IDI=integrated discrimination improvement; NRI=net reclassification index; mRS=modified Rankin Scale.

Patients were divided into 5 risk categories by CO₂CP quintiles.

Conventional model: adjusted for age, gender, body mass index, history of dyslipidemia, stroke or transient ischemic stroke, atrial fibrillation/flutter, stroke type, current smoke, antihypertensive agents, anticoagulant agents, NIHSS, high-density lipoprotein cholesterol, history of COPD, time from onset of symptoms to admission, and high sensitivity C-reactive protein on admission.