Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Univariate Comparison Between Baseline Characteristics and ASCOD Grades A1-A2 vs A0, S0, C0, O0, or D0

	A0/S0/C0/OD0 (n=484)	A1/A2 (n=998)	P-value
Age-yr, mean (SD)	58.4 (14.7)	69.8 (12.0)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	658/997 (66.0)	<0.001
Ethnicity			<0.001
Asian	80/484 (16.5)	710/998 (71.1)	
Non-Asian	404/484 (83.5)	288/998 (28.9)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	481/988 (48.7)	
TIA	326/432 (75.5)	507/988 (51.3)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	803/997 (80.5)	<0.001
Diabetes	59/480 (12.3)	241/996 (24.2)	<0.001
Dyslipidemia	287/448 (59.3)	806/998 (80.8)	<0.001
Smoke - no/total no, (%)			<0.001
Never	273/475 (57.5)	464/988 (47.0)	
Former	93/475 (19.6)	284/988 (28.7)	
Current	109/475 (22.9)	240/988 (24.3)	
Regular alcohol consumption	75/477 (15.7)	248/984 (25.2)	<0.001
Regular physical activity	148/467 (31.7)	180/974 (18.5)	<0.001
Stroke or TIA	46/484 (9.5)	204/998 (20.4)	<0.001
Coronary artery disease	0/480 (0.0)	184/995 (18.5)	<0.001
Peripheral artery disease	0/474 (0.0)	56/996 (5.6)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	96/995 (9.7)	<0.001
Congestive heart failure	0/482 (0.0)	33/995 (3.3)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	28/998 (2.8)	0.006
Atherosclerotic dyslipidemia[1]	28/349 (8.0)	90/868 (10.4)	0.21
Atherosclerotic dyslipidemia[2]	67/349 (19.2)	198/869 (22.8)	0.17
Diabetes and Atherosclerotic dyslipidemia[2]	15/482 (3.1)	73/997 (7.3)	0.001
Body-mass index, mean (SD)	26.4 (4.7)	25.9 (4.4)	0.039
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	149 (23)	<0.001
Diastolic, mean (SD)	81 (12)	80 (13)	0.63
Glucose-mg/dl, median (IQR)	99 (90-121)	104 (90-135)	0.058
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	118 (45)	0.011
HDL, mean (SD)	53 (19)	49 (16)	0.002
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	119.0 (88.0-163.0)	0.12
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	337/990 (34.0)	0.25
Living in rural area	51/465 (11.0)	96/991 (9.7)	0.45

Unemployed	35/459 (7.6)	56/975 (5.7)	0.17
Educational level			0.063
No education	14/434 (3.2)	42/959 (4.4)	
Primary education	113/434 (26.0)	284/959 (29.6)	
Secondary education	206/434 (47.5)	464/959 (48.4)	
Tertiary education	101/424 (23.3)	169/959 (17.6)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	469/944 (49.7)	
Small vessel disease	0/395 (0.0)	107/944 (11.3)	
Cardioembolism	0/395 (0.0)	116/944 (12.3)	
Other determined cause	0/395 (0.0)	41/944 (4.3)	
Undetermined	341/395 (86.3)	211/944 (22.4)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	233/911 (25.6)	
4-5	164/418 (39.2)	461/911 (50.6)	
6-7	46/418 (11.0)	217/911 (23.8)	
Acute infarction			<0.001
No	322/432 (74.5)	447/988 (45.2)	
Single	81/432 (18.8)	295/988 (29.9)	
Multiple	29/432 (6.7)	246/988 (24.9)	
PICO's score			<0.001
0	484/484 (100.0)	549/998 (55.0)	
1	0/484 (0.0)	381/998 (38.2)	
≥2	0/484 (0.0)	68/998 (6.8)	

eTable 2. Univariate Comparison Between Baseline Characteristics and ASCOD Grades A1-A2 and A3 vs A0, S0, C0, O0, or D0

	A0/S0/C0/OD0 (n=484)	A1/A2 and A3 (n=2106)	P-value
Age-yr, mean (SD)	58.4 (14.7)	69.3 (11.5)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	1332/2104 (63.3)	<0.001
Ethnicity			0.001
Asian	80/484 (16.5)	1607/2106 (76.3)	
Non-Asian	404/484 (83.5)	499/2106 (23.7)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	966/2072 (46.6)	
TIA	326/432 (75.5)	1106/2072 (53.4)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	1674/2104 (79.6)	<0.001
Diabetes	59/480 (12.3)	462/2100 (22.0)	<0.001
Dyslipidemia	287/448 (59.3)	1634/2106 (77.6)	<0.001
Smoke - no/total no, (%)			<0.001
Never	273/475 (57.5)	1006/2084 (48.3)	
Former	93/475 (19.6)	604/2084 (29.0)	
Current	109/475 (22.9)	474/2084 (22.7)	
Regular alcohol consumption	75/477 (15.7)	496/2078 (23.9)	<0.001
Regular physical activity	148/467 (31.7)	401/2057 (19.5)	<0.001
Stroke or TIA	46/484 (9.5)	413/2103 (19.6)	<0.001
Coronary artery disease	0/480 (0.0)	481/2102 (22.9)	<0.001
Peripheral artery disease	0/474 (0.0)	113/2101 (5.4)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	219/2101 (10.4)	<0.001
Congestive heart failure	0/482 (0.0)	76/2100 (3.6)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	71/2106 (3.4)	0.001
Atherosclerotic dyslipidemia[1]	28/349 (8.0)	171/1787 (9.6)	0.36
Atherosclerotic dyslipidemia[2]	67/349 (19.2)	395/1789 (22.1)	0.23
Diabetes and Atherosclerotic dyslipidemia[2]	15/482 (3.1)	136/2103 (6.5)	0.005
Body-mass index, mean (SD)	26.4 (4.7)	26.3 (4.5)	0.55
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	148 (23)	<0.001
Diastolic, mean (SD)	81 (12)	81 (13)	0.66
Glucose-mg/dl, median (IQR)	99 (90-121)	105 (92-133)	0.11
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	118 (42)	0.006
HDL, mean (SD)	53 (19)	50 (16)	0.004
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	119.0 (88.0-164.0)	0.11
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	734/2079 (35.3)	0.076
Living in rural area	51/465 (11.0)	213/2088 (10.2)	0.62

Unemployed	35/459 (7.6)	89/2050 (4.3)	0.003
Educational level			0.012
No education	14/434 (3.2)	80/1987 (4.0)	
Primary education	113/434 (26.0)	604/1987 (30.4)	
Secondary education	206/434 (47.5)	967/1987 (48.7)	
Tertiary education	101/424 (23.3)	336/1987 (16.9)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	724/1999 (36.2)	
Small vessel disease	0/395 (0.0)	371/1999 (18.6)	
Cardioembolism	0/395 (0.0)	307/1999 (15.4)	
Other determined cause	0/395 (0.0)	85/1999 (4.3)	
Undetermined	341/395 (86.3)	512/1999 (25.6)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	535/1913 (28.0)	
4-5	164/418 (39.2)	921/1913 (48.1)	
6-7	46/418 (11.0)	457/1913 (23.9)	
Acute infarction			<0.001
No	322/432 (74.5)	1007/2072 (48.6)	
Single	81/432 (18.8)	649/2072 (31.3)	
Multiple	29/432 (6.7)	416/2072 (20.1)	
PICO's score			<0.001
0	484/484 (100.0)	1244/2016 (59.1)	
1	0/484 (0.0)	703/2106 (33.4)	
≥2	0/484 (0.0)	159/2106 (7.5)	

eTable 3. Baseline Characteristics According to ASCOD Grading System S (Small Vessel Disease)

	S0 (n=2141)	S1/S2 (n=773)	S3 (n=912)	S9 (n=21)
Age-yr, mean (SD)	63.2 (13.8)	67.0 (11.5)	73.7 (10.0)	61.1 (12.9)
Male sex - no/total no, (%)	1276/2137 (59.7)	464/772 (60.1)	543/911 (59.6)	12/21 (57.1)
Ethnicity				
Asian	445/2141 (20.8)	272/773 (35.2)	160/912 (17.5)	5/21 (23.8)
Non-Asian	1696/2141 (79.2)	501/773 (64.8)	752/912 (82.5)	16/21 (76.2)
Qualifying event				
Stroke	741/2021 (36.7)	438/764 (57.3)	409/909 (45.0)	0/21 (0.0)
TIA	1280/2021 (63.3)	326/764 (42.7)	500/909 (55.0)	0/21 (0.0)
Medical history - no/total no, (%)				
Hypertension	1364/2132 (64.0)	563/773 (72.8)	765/911 (84.0)	15/21 (71.4)
Diabetes	335/2132 (15.7)	189/771 (24.5)	196/909 (21.6)	7/20 (35.0)
Dyslipidemia	1401/2141 (65.4)	590/773 (76.3)	700/912 (76.8)	18/21 (85.7)
Smoke - no/total no, (%)				
Never	1107/2118 (52.3)	425/756 (56.2)	478/906 (52.8)	14/21 (66.7)
Former	505/2118 (23.8)	148/756 (19.6)	289/906 (31.9)	0/21 (0.0)
Current	506/2118 (23.9)	183/756 (24.2)	139/906 (15.3)	7/21 (33.3)
Regular alcohol consumption	445/2115 (21.0)	141/761 (18.5)	206/904 (22.8)	6/21 (28.6)
Regular physical activity	480/2054 (23.4)	119/749 (15.9)	194/888 (21.9)	8/21 (38.1)
Stroke or TIA	323/2141 (15.1)	123/773 (15.9)	207/912 (22.7)	5/21 (23.8)
Coronary artery disease	239/2133 (11.2)	73/772 (9.5)	163/907 (18.0)	6/21 (28.6)
Peripheral artery disease	43/2122 (2.0)	22/770 (2.9)	48/906 (5.3)	0/21 (0.0)
Atrial fibrillation or flutter	204/2135 (9.6)	15/772 (1.9)	115/908 (12.7)	1/21 (4.8)
Congestive heart failure	47/2135 (2.2)	13/772 (1.7)	48/908 (5.3)	1/21 (4.8)
Clinically significant valvular disease or prosthetic heart valve	53/2141 (2.5)	13/773 (1.7)	39/912 (4.3)	0/21 (0.0)
Atherogenic dyslipidemia[1]	147/1684 (8.7)	60/637 (9.4)	63/761 (8.3)	2/9 (22.2)
Atherogenic dyslipidemia[2]	364/1685 (21.6)	144/538 (22.6)	144/761 (18.9)	3/9 (33.3)

Diabetes and Atherosclerotic dyslipidemia([2])	97/2137 (4.5)	51/772 (6.6)	47/910 (5.2)	2/21 (9.5)
Body-mass index, mean (SD)	26.5 (4.7)	26.3 (4.8)	26.0 (4.2)	27.4 (5.1)
Blood pressure-mm Hg				
Systolic, mean (SD)	143 (23)	152 (25)	147 (24)	144 (25)
Diastolic, mean (SD)	81 (13)	84 (13)	79 (14)	82 (13)
Glucose-mg/dl, median (IQR)	102 (90-127)	105 (91-130)	105 (92-130)	147 (92-207)
Cholesterol- mg/dl				
LDL, mean (SD)	120 (39)	124 (41)	115 (42)	116 (41)
HDL, mean (SD)	51 (16)	51 (16)	50 (16)	44 (15)
Triglyceride, median(IQR), mg/dl	120.0 (87.0-167.0)	119.0 (88.0-179.0)	115.5 (88.0-151.0)	143.0 (93.0-219.0)
Socio-economic factors - no/total no, (%)				
Living alone	606/2095 (28.9)	271/751 (36.1)	384/906 (42.4)	7/21 (33.3)
Living in rural area	244/2069 (11.8)	102/766 (13.3)	105/907 (11.6)	3/21 (14.3)
Unemployed	119/2035 (5.9)	36/742 (4.9)	39/900 (4.3)	1/21 (4.8)
Educational level				
No education	63/1965 (3.2)	39/699 (5.6)	57/871 (6.5)	0/21 (0.0)
Primary education	530/1965 (27.0)	232/699 (33.2)	315/871 (36.2)	3/21 (14.3)
Secondary education	996/1965 (50.7)	333/699 (47.6)	352/871 (40.4)	16/21 (76.2)
Tertiary education	376/1965 (19.1)	95/699 (13.6)	147/871 (16.9)	2/21 (9.5)
TOAST classification				
Large artery atherosclerosis	573/1931 (29.7)	0/762 (0.0)	295/846 (34.9)	8/19 (42.1)
Small vessel disease	0/1931 (0.0)	762/762 (100)	0/846 (0.0)	0/19 (0.0)
Cardioembolism	382/1931 (19.8)	0/762 (0.0)	177/846 (20.9)	3/19 (15.8)
Other determined cause	156/1931 (8.1)	0/762 (0.0)	40/846 (4.7)	0/19 (0.0)
Undetermined	820/1931 (42.5)	0/762 (0.0)	334/846 (39.5)	8/19 (42.1)
ABCD2 score				
0-3	722/1861 (38.8)	145/708 (20.5)	224/828 (27.0)	12/20 (60.0)
4-5	832/1861 (44.7)	358/708 (50.6)	447/828 (54.0)	4/20 (20.0)
6-7	307/1861 (16.5)	205/708 (28.9)	157/828 (19.0)	4/20 (20.0)

Acute infarction				
No	1244/2021 (61.6)	299/764 (39.1)	421/909 (46.3)	0/21 (0.0)
Single	493/2021 (24.4)	366/764 (47.9)	266/909 (29.3)	0/21 (0.0)
Multiple	284/2021 (14.0)	99/764 (13.0)	222/909 (24.4)	0/21 (0.0)
PICO's score				
0	2141/2141 (100.0)	392/773 (50.7)	0/912 (0.0)	21/21 (100.0)
1	0/2141 (0.0)	240/773 (31.1)	821/912 (90.0)	0/21 (0.0)
≥2	0/2141 (0.0)	141/773 (18.2)	91/912 (10.0)	0/21 (0.0)
Score at discharge				
NIHSS at discharge				
0	1615/1893 (85.3)	483/728 (66.4)	674/835 (80.7)	18/20 (90.0)
1-4	268/1893 (14.2)	245/728 (33.6)	149/835 (17.8)	2/20 (10.0)
>5	10/1893 (0.5)	0/728 (0.0)	12/835 (1.5)	0/20 (0.0)
RANKIN at discharge >1 - no/total no, (%)	28/1902 (1.5)	9/743 (1.2)	32/840 (3.8)	0/20 (0.0)

[1] Define as triglycerides >200 mg/dL and HDL ≤40 mg/dL for men (HDL ≤50 mg/dL for women);
[2] Define as triglycerides >150 mg/dL an HDL ≤50 mg/dL

eTable 4. Univariate Comparison Between Baseline Characteristics and ASCOD Grades S1-S2 vs S0

	S0 (n=2141)	S1/S2 (n=773)	P-value
Age-yr, mean (SD)	63.2 (13.8)	67.0 (11.5)	<0.001
Male sex - no/total no, (%)	1276/2137 (59.7)	464/772 (60.1)	0.85
Ethnicity			<0.001
Asian	445/2141 (20.8)	272/773 (35.2)	
Non-Asian	1696/2141 (79.2)	501/773 (64.8)	
Qualifying event			<0.001
Stroke	741/2021 (36.7)	438/764 (57.3)	
TIA	1280/2021 (63.3)	326/764 (42.7)	
Medical history - no/total no, (%)			
Hypertension	1364/2132 (64.0)	563/773 (72.8)	<0.001
Diabetes	335/2132 (15.7)	189/771 (24.5)	<0.001
Dyslipidemia	1401/2141 (65.4)	590/773 (76.3)	<0.001
Smoke - no/total no, (%)			0.047
Never	1107/2118 (52.3)	425/756 (56.2)	
Former	505/2118 (23.8)	148/756 (19.6)	
Current	506/2118 (23.9)	183/756 (24.2)	
Regular alcohol consumption	445/2115 (21.0)	141/761 (18.5)	0.14
Regular physical activity	480/2054 (23.4)	119/749 (15.9)	<0.001
Stroke or TIA	323/2141 (15.1)	123/773 (15.9)	0.58
Coronary artery disease	239/2133 (11.2)	73/772 (9.5)	0.18
Peripheral artery disease	43/2122 (2.0)	22/770 (2.9)	0.18
Atrial fibrillation or flutter	204/2135 (9.6)	15/772 (1.9)	<0.001
Congestive heart failure	47/2135 (2.2)	13/772 (1.7)	0.39
Clinically significant valvular disease or prosthetic heart valve	53/2141 (2.5)	13/773 (1.7)	0.20
Atherogenic dyslipidemia([1])	147/1684 (8.7)	60/637 (9.4)	0.60
Atherogenic dyslipidemia([2])	364/1685 (21.6)	144/538 (22.6)	0.61
Diabetes and Atherogenic dyslipidemia([2])	97/2137 (4.5)	51/772 (6.6)	0.025
Body-mass index, mean (SD)	26.5 (4.7)	26.3 (4.8)	0.36
Blood pressure-mm Hg			
Systolic, mean (SD)	143 (23)	152 (25)	<0.001
Diastolic, mean (SD)	81 (13)	84 (13)	<0.001
Glucose-mg/dl, median (IQR)	102 (90-127)	105 (91-130)	0.096
Cholesterol- mg/dl			
LDL, mean (SD)	120 (39)	124 (41)	0.022
HDL, mean (SD)	51 (16)	51 (16)	0.87
Triglyceride, median(IQR), mg/dl	120.0 (87.0-167.0)	119.0 (88.0-179.0)	0.19
Socio-economic factors - no/total no, (%)			
Living alone	606/2095 (28.9)	271/751 (36.1)	<0.001
Living in rural area	244/2069 (11.8)	102/766 (13.3)	0.27

Unemployed	119/2035 (5.9)	36/742 (4.9)	0.31
Educational level			<0.001
No education	63/1965 (3.2)	39/699 (5.6)	
Primary education	530/1965 (27.0)	232/699 (33.2)	
Secondary education	996/1965 (50.7)	333/699 (47.6)	
Tertiary education	376/1965 (19.1)	95/699 (13.6)	
TOAST classification			<0.001
Large artery atherosclerosis	573/1931 (29.7)	0/762 (0.0)	
Small vessel disease	0/1931 (0.0)	762/762 (100)	
Cardioembolism	382/1931 (19.8)	0/762 (0.0)	
Other determined cause	156/1931 (8.1)	0/762 (0.0)	
Undetermined	820/1931 (42.5)	0/762 (0.0)	
ABCD2 score			<0.001
0-3	722/1861 (38.8)	145/708 (20.5)	
4-5	832/1861 (44.7)	358/708 (50.6)	
6-7	307/1861 (16.5)	205/708 (28.9)	
Acute infarction			<0.001
No	1244/2021 (61.6)	299/764 (39.1)	
Single	493/2021 (24.4)	366/764 (47.9)	
Multiple	284/2021 (14.0)	99/764 (13.0)	
PICO's score			<0.001
0	2141/2141 (100.0)	392/773 (50.7)	
1	0/2141 (0.0)	240/773 (31.1)	
≥2	0/2141 (0.0)	141/773 (18.2)	

eTable 5. Multivariable Association Between Baseline Characteristics and ASCOD Grades S1-S2 vs S0

	OR (95%CI)	P-value
Acute infarction		
No	1.00 (reference)	-
Single	2.54 (2.07-3.12)	<0.001
Multiple	1.05 (0.79-1.39)	0.74
Atrial fibrillation or flutter	0.16 (0.09-0.27)	<0.001
Ethnicity		
Non-Asian	1.00 (ref.)	-
Asian	1.84 (1.50-2.26)	<0.001
Age, per 10 years increase	1.22 (1.13-1.32)	<0.001
Systolic, per 24 mm Hg increase	1.26 (1.14-1.39)	<0.001
Living alone	1.59 (1.30-1.94)	<0.001
Regular physical activity	0.60 (0.47-0.77)	<0.001
Dyslipidemia	1.44 (1.17-1.77)	0.001
Diabetes	1.41 (1.12-1.77)	0.003
ABCD2 score		
0-3	1.00 (ref.)	-
4-5	1.38 (1.09-1.74)	0.008
6-7	1.50 (1.12-2.00)	0.006
LDL, per 40 mg/dL increase	1.13 (1.01-1.26)	0.029

eTable 6. Univariate Comparison Between Baseline Characteristics and ASCOD Grades S1-S2 and S3 vs S0

	S0 (n=2141)	S1/S2/S3 (n=1685)	P-value
Age-yr, mean (SD)	63.2 (13.8)	70.6 (11.2)	<0.001
Male sex - no/total no, (%)	1276/2137 (59.7)	1007/1683 (59.8)	0.94
Ethnicity			<0.001
Asian	445/2141 (20.8)	432/1685 (25.6)	
Non-Asian	1696/2141 (79.2)	1253/1685 (74.4)	
Qualifying event			<0.001
Stroke	741/2021 (36.7)	847/1673 (50.6)	
TIA	1280/2021 (63.3)	826/1673 (49.4)	
Medical history - no/total no, (%)			
Hypertension	1364/2132 (64.0)	1328/1684 (78.9)	<0.001
Diabetes	335/2132 (15.7)	385/1680 (22.9)	<0.001
Dyslipidemia	1401/2141 (65.4)	1290/1685 (76.6)	<0.001
Smoke - no/total no, (%)			0.003
Never	1107/2118 (52.3)	903/1662 (54.3)	
Former	505/2118 (23.8)	437/1662 (26.3)	
Current	506/2118 (23.9)	322/1662 (19.4)	
Regular alcohol consumption	445/2115 (21.0)	347/1665 (20.8)	0.88
Regular physical activity	480/2054 (23.4)	313/1637 (19.1)	0.002
Stroke or TIA	323/2141 (15.1)	330/1685 (19.6)	<0.001
Coronary artery disease	239/2133 (11.2)	236/1679 (14.1)	0.008
Peripheral artery disease	43/2122 (2.0)	70/1676 (4.2)	<0.001
Atrial fibrillation or flutter	204/2135 (9.6)	130/1680 (7.7)	0.049
Congestive heart failure	47/2135 (2.2)	61/1680 (3.6)	0.008
Clinically significant valvular disease or prosthetic heart valve	53/2141 (2.5)	52/1685 (3.1)	0.25
Atherogenic dyslipidemia[1]	147/1684 (8.7)	123/1398 (8.8)	0.95
Atherogenic dyslipidemia[2]	364/1685 (21.6)	288/1399 (20.6)	0.49
Diabetes and Atherogenic dyslipidemia[2]	97/2137 (4.5)	98/1682 (5.8)	0.073
Body-mass index, mean (SD)	26.5 (4.7)	26.1 (4.5)	0.016
Blood pressure-mm Hg			
Systolic, mean (SD)	143 (23)	149 (24)	<0.001
Diastolic, mean (SD)	81 (13)	81 (14)	0.55
Glucose-mg/dl, median (IQR)	102 (90-127)	105 (92-130)	0.27
Cholesterol- mg/dl			
LDL, mean (SD)	120 (39)	119 (42)	0.69
HDL, mean (SD)	51 (16)	51 (16)	0.84
Triglyceride, median(IQR), mg/dl	120.0 (87.0-167.0)	115.0 (88.0-160.0)	0.67
Socio-economic factors - no/total no, (%)			
Living alone	606/2095 (28.9)	655/1657 (39.5)	<0.001
Living in rural area	244/2069 (11.8)	207/1673 (12.4)	0.59
Unemployed	119/2035 (5.9)	75/1642 (4.6)	0.084

Educational level			<0.001
No education	63/1965 (3.2)	96/1570 (6.1)	
Primary education	530/1965 (27.0)	547/1570 (34.8)	
Secondary education	996/1965 (50.7)	685/1570 (43.6)	
Tertiary education	376/1965 (19.1)	242/1570 (15.4)	
TOAST classification			<0.001
Large artery atherosclerosis	573/1931 (29.7)	295/1608 (18.4)	
Small vessel disease	0/1931 (0.0)	762/1608 (47.4)	
Cardioembolism	382/1931 (19.8)	177/1608 (11.0)	
Other determined cause	156/1931 (8.1)	40/1608 (2.5)	
Undetermined	820/1931 (42.5)	334/1608 (20.8)	
ABCD2 score			<0.001
0-3	722/1861 (38.8)	369/1536 (24.0)	
4-5	832/1861 (44.7)	805/1536 (52.4)	
6-7	307/1861 (16.5)	362/1536 (23.6)	
Acute infarction			<0.001
No	1244/2021 (61.6)	720/1673 (43.0)	
Single	493/2021 (24.4)	632/1673 (37.8)	
Multiple	284/2021 (14.0)	321/1673 (19.2)	
PICO's score			<0.001
0	2141/2141 (100.0)	392/1685 (23.2)	
1	0/2141 (0.0)	1061/1685 (60.0)	
≥2	0/2141 (0.0)	232/1685 (13.8)	

eTable 7. Multivariable Association Between Baseline Characteristics and ASCOD Grades S1-S2 and S3 vs S0

	OR (95%CI)	P-value
Age, per 10 years increase	1.55 (1.45-1.65)	<0.001
Living alone	1.60 (0.38-1.86)	<0.001
Acute infarction		
No	1.00 (ref.)	-
Single	3.13 (2.14-4.57)	<0.001
Multiple	2.30 (1.60-333)	<0.001
Atrial fibrillation or flutter	0.55 (0.43-0.70)	<0.001
Dyslipidemia	1.39 (1.19-1.64)	<0.001
Systolic, per 24 mm Hg increase	1.14 (1.06-1.23)	0.001
Hypertension	1.33 (1.12-1.58)	0.001
Ethnicity		
Non-Asian	1.00 (ref.)	-
Asian	1.32 (1.11-1.57)	0.001
Diabetes	1.25 (1.05-1.50)	0.012
Regular physical activity	0.80 (0.66-0.96)	0.015
Peripheral artery disease	1.67 (1.10-2.52)	0.015
Qualifying event		
TIA	1.00 (ref.)	-
Stroke	0.67 (0.47-0.96)	0.032

eTable 8. Univariate Comparison Between Baseline Characteristics and ASCOD Grades S1-S2 vs A0, S0, C0, O0, and D0

	A0/S0/C0/OD0 (n=484)	S1/S2 (n=773)	P-value
Age-yr, mean (SD)	58.4 (14.7)	67.0 (11.5)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	464/772 (60.1)	0.004
Ethnicity			<0.001
Asian	80/484 (16.5)	272/773 (35.2)	
Non-Asian	404/484 (83.5)	501/773 (64.8)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	438/764 (57.3)	
TIA	326/432 (75.5)	326/764 (42.7)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	563/773 (72.8)	<0.001
Diabetes	59/480 (12.3)	189/771 (24.5)	<0.001
Dyslipidemia	287/448 (59.3)	590/773 (76.3)	<0.001
Smoke - no/total no, (%)			0.87
Never	273/475 (57.5)	425/756 (56.2)	
Former	93/475 (19.6)	148/756 (19.6)	
Current	109/475 (22.9)	183/756 (24.2)	
Regular alcohol consumption	75/477 (15.7)	141/761 (18.5)	0.21
Regular physical activity	148/467 (31.7)	119/749 (15.9)	<0.001
Stroke or TIA	46/484 (9.5)	123/773 (15.9)	0.001
Coronary artery disease	0/480 (0.0)	73/772 (9.5)	<0.001
Peripheral artery disease	0/474 (0.0)	22/770 (2.9)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	15/772 (1.9)	0.12
Congestive heart failure	0/482 (0.0)	13/772 (1.7)	0.003
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	13/773 (1.7)	0.10
Atherogenic dyslipidemia([1])	28/349 (8.0)	60/637 (9.4)	0.46
Atherogenic dyslipidemia([2])	67/349 (19.2)	144/538 (22.6)	0.22
Diabetes and Atherogenic dyslipidemia([2])	15/482 (3.1)	51/772 (6.6)	0.007
Body-mass index, mean (SD)	26.4 (4.7)	26.3 (4.8)	0.70
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	152 (25)	<0.001
Diastolic, mean (SD)	81 (12)	84 (13)	<0.001
Glucose-mg/dl, median (IQR)	99 (90-121)	105 (91-130)	0.99
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	124 (41)	0.72
HDL, mean (SD)	53 (19)	51 (16)	0.070
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	119.0 (88.0-179.0)	0.038
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	271/751 (36.1)	0.068
Living in rural area	51/465 (11.0)	102/766 (13.3)	0.23
Unemployed	35/459 (7.6)	36/742 (4.9)	0.048

Educational level			<0.001
No education	14/434 (3.2)	39/699 (5.6)	
Primary education	113/434 (26.0)	232/699 (33.2)	
Secondary education	206/434 (47.5)	333/699 (47.6)	
Tertiary education	101/424 (23.3)	95/699 (13.6)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	0/762 (0.0)	
Small vessel disease	0/395 (0.0)	762/762 (100)	
Cardioembolism	0/395 (0.0)	0/762 (0.0)	
Other determined cause	0/395 (0.0)	0/762 (0.0)	
Undetermined	341/395 (86.3)	0/762 (0.0)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	145/708 (20.5)	
4-5	164/418 (39.2)	358/708 (50.6)	
6-7	46/418 (11.0)	205/708 (28.9)	
Acute infarction			<0.001
No	322/432 (74.5)	299/764 (39.1)	
Single	81/432 (18.8)	366/764 (47.9)	
Multiple	29/432 (6.7)	99/764 (13.0)	
PICO's score			<0.001
0	484/484 (100.0)	392/773 (50.7)	
1	0/484 (0.0)	240/773 (31.1)	
≥2	0/484 (0.0)	141/773 (18.2)	

eTable 9. Univariate Comparison Between Baseline Characteristics and ASCOD Grades S1-S2 and S3 vs A0, S0, C0, O0, and D0

	A0/S0/C0/OD0 (n=484)	S1/S2/S3 (n=1685)	P-value
Age-yr, mean (SD)	58.4 (14.7)	70.6 (11.2)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	1007/1683 (59.8)	0.002
Ethnicity			<0.001
Asian	80/484 (16.5)	432/1685 (25.6)	
Non-Asian	404/484 (83.5)	1253/1685 (74.4)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	847/1673 (50.6)	
TIA	326/432 (75.5)	826/1673 (49.4)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	1328/1684 (78.9)	<0.001
Diabetes	59/480 (12.3)	385/1680 (22.9)	<0.001
Dyslipidemia	287/448 (59.3)	1290/1685 (76.6)	<0.001
Smoke - no/total no, (%)			0.008
Never	273/475 (57.5)	903/1662 (54.3)	
Former	93/475 (19.6)	437/1662 (26.3)	
Current	109/475 (22.9)	322/1662 (19.4)	
Regular alcohol consumption	75/477 (15.7)	347/1665 (20.8)	0.013
Regular physical activity	148/467 (31.7)	313/1637 (19.1)	<0.001
Stroke or TIA	46/484 (9.5)	330/1685 (19.6)	<0.001
Coronary artery disease	0/480 (0.0)	236/1679 (14.1)	<0.001
Peripheral artery disease	0/474 (0.0)	70/1676 (4.2)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	130/1680 (7.7)	<0.001
Congestive heart failure	0/482 (0.0)	61/1680 (3.6)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	52/1685 (3.1)	0.002
Atherogenic dyslipidemia[1]	28/349 (8.0)	123/1398 (8.8)	0.64
Atherogenic dyslipidemia[2]	67/349 (19.2)	288/1399 (20.6)	0.56
Diabetes and Atherogenic dyslipidemia[2]	15/482 (3.1)	98/1682 (5.8)	0.018
Body-mass index, mean (SD)	26.4 (4.7)	26.1 (4.5)	0.23
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	149 (24)	<0.001
Diastolic, mean (SD)	81 (12)	81 (14)	0.29
Glucose-mg/dl, median (IQR)	99 (90-121)	105 (92-130)	0.49
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	119 (42)	0.021
HDL, mean (SD)	53 (19)	51 (16)	0.029
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	115.0 (88.0-160.0)	0.28
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	655/1657 (39.5)	0.001
Living in rural area	51/465 (11.0)	207/1673 (12.4)	0.41
Unemployed	35/459 (7.6)	75/1642 (4.6)	0.009

Educational level			<0.001
No education	14/434 (3.2)	96/1570 (6.1)	
Primary education	113/434 (26.0)	547/1570 (34.8)	
Secondary education	206/434 (47.5)	685/1570 (43.6)	
Tertiary education	101/424 (23.3)	242/1570 (15.4)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	295/1608 (18.4)	
Small vessel disease	0/395 (0.0)	762/1608 (47.4)	
Cardioembolism	0/395 (0.0)	177/1608 (11.0)	
Other determined cause	0/395 (0.0)	40/1608 (2.5)	
Undetermined	341/395 (86.3)	334/1608 (20.8)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	369/1536 (24.0)	
4-5	164/418 (39.2)	805/1536 (52.4)	
6-7	46/418 (11.0)	362/1536 (23.6)	
Acute infarction			<0.001
No	322/432 (74.5)	720/1673 (43.0)	
Single	81/432 (18.8)	632/1673 (37.8)	
Multiple	29/432 (6.7)	321/1673 (19.2)	
PICO's score			<0.001
0	484/484 (100.0)	392/1685 (23.2)	
1	0/484 (0.0)	1061/1685 (60.0)	
≥2	0/484 (0.0)	232/1685 (13.8)	

eTable 10. Baseline Characteristics According to ASCOD Grading System C (Cardiac Pathology)

	C0 (n=2733)	C1/C2 (n=800)	C3 (n=226)	C9 (n=88)
Age-yr, mean (SD)	65.9 (13.0)	70.2 (12.4)	61.5 (15.0)	63.2 (14.6)
Male sex - no/total no, (%)	1627/2727 (59.7)	477/800 (59.6)	138/226 (61.1)	53/88 (60.2)
Ethnicity				
Asian	685/2733 (25.1)	146/800 (18.3)	23/226 (10.2)	28/88 (31.8)
Non-Asian	2048/2733 (74.9)	654/800 (81.7)	203/226 (89.8)	60/88 (68.2)
Qualifying event				
Stroke	1082/2602 (41.6)	388/787 (49.3)	94/225 (41.8)	24/80 (30.0)
TIA	1520/2602 (58.4)	399/787 (50.7)	131/225 (58.2)	56/80 (70.0)
Medical history - no/total no, (%)				
Hypertension	1882/2725 (69.1)	638/798 (80.0)	127/226 (56.2)	60/88 (68.2)
Diabetes	544/2723 (20.0)	142/797 (17.8)	27/225 (12.0)	14/87 (16.1)
Dyslipidemia	1956/2733 (71.6)	551/800 (68.9)	155/226 (68.6)	47/88 (53.4)
Smoke - no/total no, (%)				
Never	1394/2699 (51.6)	459/791 (58.0)	118/223 (52.9)	53/88 (60.2)
Former	660/2699 (24.5)	213/791 (26.9)	54/223 (24.2)	15/88 (17.1)
Current	645/2699 (23.9)	119/791 (15.1)	51/223 (22.9)	20/88 (22.7)
Regular alcohol consumption	569/2699 (21.1)	169/789 (21.4)	51/225 (22.7)	9/88 (10.2)
Regular physical activity	572/2624 (21.8)	148/780 (19.0)	69/220 (31.4)	12/88 (13.6)
Stroke or TIA	457/2733 (16.7)	148/800 (18.5)	31/226 (13.7)	22/88 (25.0)
Coronary artery disease	268/2724 (9.8)	185/796 (23.2)	13/225 (5.8)	15/88 (17.1)
Peripheral artery disease	71/2713 (2.6)	35/795 (4.4)	3/223 (1.4)	4/88 (4.6)
Atrial fibrillation or flutter	49/2728 (1.8)	281/794 (35.4)	3/226 (1.3)	2/88 (2.3)
Congestive heart failure	39/2727 (1.4)	65/795 (8.2)	4/226 (1.8)	1/88 (1.1)
Clinically significant valvular disease or prosthetic heart valve	38/2733 (1.4)	67/800 (8.4)	0/226 (0.0)	0/88 (0.0)
Atherogenic dyslipidemia([1])	210/2182 (9.6)	42/653 (6.4)	12/205 (5.9)	8/51 (15.7)
Atherogenic dyslipidemia([2])	495/2184 (22.7)	119/653 (18.2)	27/205 (13.2)	14/51 (27.5)

Diabetes and Atherogenic dyslipidemia(^{2})	146/2726 (5.4)	40/800 (5.0)	7/226 (3.1)	4/88 (4.6)
Body-mass index, mean (SD)	26.4 (4.6)	26.4 (4.6)	25.9 (4.0)	63.2 (14.6)
Blood pressure-mm Hg				
Systolic, mean (SD)	147 (23)	144 (25)	142 (22)	148 (22)
Diastolic, mean (SD)	82 (13)	79 (15)	80 (13)	86 (15)
Glucose-mg/dl, median (IQR)	104 (91-131)	104 (90-126)	98 (89-114)	101 (91-124)
Cholesterol- mg/dl				
LDL, mean (SD)	121 (42)	112 (38)	119 (35)	117 (38)
HDL, mean (SD)	51 (17)	50 (15)	54 (17)	45 (12)
Triglyceride, median(IQR), mg/dl	121.0 (89.0-169.0)	110.0 (83.0-156.0)	106.0 (77.0-141.0)	133.0 (93.0-188.0)
Socio-economic factors - no/total no, (%)				
Living alone	927/2678 (34.6)	248/791 (31.4)	72/219 (32.9)	21/85 (24.7)
Living in rural area	338/2662 (12.7)	97/792 (12.3)	10/222 (4.5)	9/87 (10.3)
Unemployed	145/2616 (5.5)	38/777 (4.9)	8/219 (3.7)	4/86 (4.7)
Educational level				
No education	108/2510 (4.3)	44/748 (5.9)	3/215 (1.4)	4/83 (4.8)
Primary education	769/2510 (30.6)	245/748 (32.8)	47/215 (21.9)	19/83 (22.9)
Secondary education	1203/2510 (47.9)	337/748 (45.0)	104/215 (48.4)	53/83 (63.9)
Tertiary education	430/2510 (17.1)	122/748 (16.3)	61/215 (28.4)	7/83 (8.4)
TOAST classification				
Large artery atherosclerosis	743/2507 (29.6)	68/760 (8.9)	38/220 (17.3)	27/71 (38.0)
Small vessel disease	665/2507 (26.5)	40/760 (5.3)	43/220 (19.5)	14/71 (19.7)
Cardioembolism	0/2507 (0.0)	562/760 (73.9)	0/220 (0.0)	0/71 (0.0)
Other determined cause	166/2507 (6.6)	8/760 (1.1)	14/220 (6.4)	8/71 (11.3)
Undetermined	33/2507 (37.2)	82/760 (10.8)	125/220 (56.8)	22/71 (31.0)
ABCD2 score				
0-3	805/2423 (33.2)	183/704 (26.0)	92/211 (43.6)	23/79 (29.1)
4-5	1131/2423 (46.7)	381/704 (54.1)	88/211 (41.7)	41/79 (51.9)
6-7	487/2423 (20.1)	140/704 (19.9)	31/211 (14.7)	15/79 (19.0)

Acute infarction				
No	1419/2602 (54.5)	371/787 (47.2)	121/225 (53.8)	53/80 (66.3)
Single	784/2602 (30.1)	245/787 (31.1)	78/225 (34.7)	18/80 (22.5)
Multiple	399/2602 (15.3)	171/787 (21.7)	26/225 (11.5)	9/80 (11.2)
PICO's score				
0	1792/2733 (64.6)	526/800 (65.8)	159/226 (70.4)	77/88 (87.5)
1	762/2733 (27.9)	241/800 (30.1)	50/226 (22.1)	8/88 (9.1)
≥2	179/2733 (6.5)	33/800 (4.1)	17/226 (7.5)	3/88 (3.4)
Score at discharge				
NIHSS at discharge				
0	1942/2441 (79.6)	599/739 (81.1)	187/219 (85.4)	62/77 (80.5)
1-4	483/2441 (19.8)	134/739 (18.1)	32/219 (14.6)	15/77 (19.5)
>5	16/2441 (0.6)	6/739 (0.8)	0/219 (0.0)	0/77 (0.0
RANKIN at discharge >1 - no/total no, (%)	44/2447 (1.8)	25/763 (3.3)	0/219 (0.0)	0/76 (0.0)

(^{1}) Define as triglycerides >200 mg/dL and HDL ≤40 mg/dL for men (HDL ≤50 mg/dL for women);

(^{2}) Define as triglycerides >150 mg/dL an HDL ≤50 mg/dL

eTable 11. Five-Year Event Rates According to ASCOD Classification C (Cardiac Pathology)

	C0 (n=2733)	C1/C2 (n=800)	C3 (n=226)	P-value[1]	P-value[2]
Major cardiovascular event	315 (12.3) (11.0 to 13.6)	125 (16.6) (14.1 to 19.4)	18 (8.3) (5.1 to 12.5)	0.001[a]	0.001 [a]
Recurrent stroke	232 (9.0)	87 (11.5)	18 (8.3)	0.090 [a]	0.034 [a]
Death	231 (9.2)	124 (17.2)	7 (3.4)	<0.001[b]	<0.001 [b]

Values are number of events (event rate expressed as % estimated from Kaplan-Meier or Kalbfleisch and Prentice estimates for time to event outcomes).

[1] P-value for comparing the three groups; [2] P-value for comparing C0 vs. C1/C2

P-value were calculated using Gray's test ([a]) or log-rank test ([b])

eTable 12. Effect Sizes Associated With ASCOD Classification C1-C2 and C3 Compared With C0

	C0	C1/C2		C3	
		HR (95% CI)	P	HR (95% CI)	P
Major cardiovascular event	1.00 (reference)	1.40 (1.14-1.72)	0.001	068 (0.42-1.10)	0.12
Recurrent stroke	1.00 (reference)	1.31 (1.02-1.67)	0.034	0.94 (0.58-1.52)	0.80
Death	1.00 (reference)	1.94 (1.56-2.41)	<0.001	0.35 (0.17-0.75)	0.006

Abbreviations: CI=confidence interval; HR=hazard ratio

eTable 13. Univariate Comparison Between Baseline Characteristics and ASCOD Grades C1-C2 vs C0

	C0 (n=2733)	C1/C2 (n=800)	P-value
Age-yr, mean (SD)	65.9 (13.0)	70.2 (12.4)	<0.001
Male sex - no/total no, (%)	1627/2727 (59.7)	477/800 (59.6)	0.98
Ethnicity			<0.001
Asian	685/2733 (25.1)	146/800 (18.3)	
Non-Asian	2048/2733 (74.9)	654/800 (81.7)	
Qualifying event			<0.001
Stroke	1082/2602 (41.6)	388/787 (49.3)	
TIA	1520/2602 (58.4)	399/787 (50.7)	
Medical history - no/total no, (%)			
Hypertension	1882/2725 (69.1)	638/798 (80.0)	<0.001
Diabetes	544/2723 (20.0)	142/797 (17.8)	0.18
Dyslipidemia	1956/2733 (71.6)	551/800 (68.9)	0.14
Smoke - no/total no, (%)			<0.001
Never	1394/2699 (51.6)	459/791 (58.0)	
Former	660/2699 (24.5)	213/791 (26.9)	
Current	645/2699 (23.9)	119/791 (15.1)	
Regular alcohol consumption	569/2699 (21.1)	169/789 (21.4)	0.84
Regular physical activity	572/2624 (21.8)	148/780 (19.0)	0.090
Stroke or TIA	457/2733 (16.7)	148/800 (18.5)	0.24
Coronary artery disease	268/2724 (9.8)	185/796 (23.2)	<0.001
Peripheral artery disease	71/2713 (2.6)	35/795 (4.4)	0.010
Atrial fibrillation or flutter	49/2728 (1.8)	281/794 (35.4)	<0.001
Congestive heart failure	39/2727 (1.4)	65/795 (8.2)	<0.001
Clinically significant valvular disease or prosthetic heart valve	38/2733 (1.4)	67/800 (8.4)	<0.001
Atherogenic dyslipidemia[1]	210/2182 (9.6)	42/653 (6.4)	0.012
Atherogenic dyslipidemia[2]	495/2184 (22.7)	119/653 (18.2)	0.016
Diabetes and Atherogenic dyslipidemia[2]	146/2726 (5.4)	40/800 (5.0)	0.69
Body-mass index, mean (SD)	26.4 (4.6)	26.4 (4.6)	0.66
Blood pressure-mm Hg			
Systolic, mean (SD)	147 (23)	144 (25)	0.001
Diastolic, mean (SD)	82 (13)	79 (15)	0.001
Glucose-mg/dl, median (IQR)	104 (91-131)	104 (90-126)	0.23
Cholesterol- mg/dl			
LDL, mean (SD)	121 (42)	112 (38)	<0.001
HDL, mean (SD)	51 (17)	50 (15)	0.49
Triglyceride, median(IQR), mg/dl	121.0 (89.0-169.0)	110.0 (83.0-156.0)	<0.001
Socio-economic factors - no/total no, (%)			
Living alone	927/2678 (34.6)	248/791 (31.4)	0.089
Living in rural area	338/2662 (12.7)	97/792 (12.3)	0.74
Unemployed	145/2616 (5.5)	38/777 (4.9)	0.48

Educational level			0.16
No education	108/2510 (4.3)	44/748 (5.9)	
Primary education	769/2510 (30.6)	245/748 (32.8)	
Secondary education	1203/2510 (47.9)	337/748 (45.0)	
Tertiary education	430/2510 (17.1)	122/748 (16.3)	
TOAST classification			<0.001
Large artery atherosclerosis	743/2507 (29.6)	68/760 (8.9)	
Small vessel disease	665/2507 (26.5)	40/760 (5.3)	
Cardioembolism	0/2507 (0.0)	562/760 (73.9)	
Other determined cause	166/2507 (6.6)	8/760 (1.1)	
Undetermined	33/2507 (37.2)	82/760 (10.8)	
ABCD2 score			0.001
0-3	805/2423 (33.2)	183/704 (26.0)	
4-5	1131/2423 (46.7)	381/704 (54.1)	
6-7	487/2423 (20.1)	140/704 (19.9)	
Acute infarction			<0.001
No	1419/2602 (54.5)	371/787 (47.2)	
Single	784/2602 (30.1)	245/787 (31.1)	
Multiple	399/2602 (15.3)	171/787 (21.7)	
PICO's score			0.028
0	1792/2733 (64.6)	526/800 (65.8)	
1	762/2733 (27.9)	241/800 (30.1)	
≥2	179/2733 (6.5)	33/800 (4.1)	

eTable 14. Multivariable Association Between Baseline Characteristics and ASCOD Grades C1-C2 vs C0

	OR (95%CI)	P-value
Atrial fibrillation or flutter	23.1 (16.6-32.0)	<0.001
Qualifying event		
TIA	1.00 (ref.)	-
Stroke	1.75 (1.44-2.14)	<0.001
Coronary artery disease	1.91 (1.48-2.46)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3.45 (2.09-5.71)	<0.001
Ethnicity		
Non-Asian	1.00 (ref.)	-
Asian	0.60 (0.47-0.77)	<0.001
Congestive heart failure	2.51 (1.51-4.17)	<0.001
Age, per 10 years increase	1.15 (1.06-1.25)	0.001
Systolic, per 24 mm Hg increase	0.85 (0.76-0.95)	0.004
Triglycerides, per 86 mg/dL increase	0.84 (0.74-0.95)	0.005
PICO's score		
0	1.00 (ref.)	-
1	0.79 (0.64-0.99)	0.040
≥2	0.52 (0.33-0.82)	0.005
Living alone	0.79 (0.64-0.97)	0.021

eTable 15. Univariate Comparison Between Baseline Characteristics and ASCOD Grades C1-C2 and C3 vs C0

	C0 (n=2733)	C1/C2/C3 (n=1026)	P-value
Age-yr, mean (SD)	65.9 (13.0)	68.3 (13.5)	<0.001
Male sex - no/total no, (%)	1627/2727 (59.7)	615/1026 (59.9)	0.88
Ethnicity			<0.001
Asian	685/2733 (25.1)	169/1026 (16.5)	
Non-Asian	2048/2733 (74.9)	857/1026 (83.5)	
Qualifying event			0.001
Stroke	1082/2602 (41.6)	582/1012 (47.6)	
TIA	1520/2602 (58.4)	530/1012 (52.4)	
Medical history - no/total no, (%)			
Hypertension	1882/2725 (69.1)	765/1024 (74.7)	0.001
Diabetes	544/2723 (20.0)	169/1022 (16.5)	0.017
Dyslipidemia	1956/2733 (71.6)	706/1026 (68.8)	0.097
Smoke - no/total no, (%)			<0.001
Never	1394/2699 (51.6)	577/1014 (56.9)	
Former	660/2699 (24.5)	267/1014 (26.3)	
Current	645/2699 (23.9)	170/1014 (16.8)	
Regular alcohol consumption	569/2699 (21.1)	220/1014 (21.7)	0.68
Regular physical activity	572/2624 (21.8)	217/1000 (21.7)	0.95
Stroke or TIA	457/2733 (16.7)	179/1026 (17.5)	0.60
Coronary artery disease	268/2724 (9.8)	198/1021 (19.4)	<0.001
Peripheral artery disease	71/2713 (2.6)	38/1018 (3.7)	0.071
Atrial fibrillation or flutter	49/2728 (1.8)	284/1020 (27.8)	<0.001
Congestive heart failure	39/2727 (1.4)	69/1021 (6.8)	<0.001
Clinically significant valvular disease or prosthetic heart valve	38/2733 (1.4)	67/1026 (6.5)	<0.001
Atherogenic dyslipidemia([1])	210/2182 (9.6)	54/858 (6.3)	0.003
Atherogenic dyslipidemia([2])	495/2184 (22.7)	146/858	0.001
Diabetes and Atherogenic dyslipidemia([2])	146/2726 (5.4)	47/1026 (4.6)	0.34
Body-mass index, mean (SD)	26.4 (4.6)	26.3 (4.5)	0.83
Blood pressure-mm Hg			
Systolic, mean (SD)	147 (23)	143 (24)	<0.001
Diastolic, mean (SD)	82 (13)	80 (15)	0.001
Glucose-mg/dl, median (IQR)	104 (91-131)	103 (90-124)	0.064
Cholesterol- mg/dl			
LDL, mean (SD)	121 (42)	114 (38)	<0.001
HDL, mean (SD)	51 (17)	51 (16)	0.49
Triglyceride, median(IQR), mg/dl	121.0 (89.0-169.0)	109.0 (82.0-151.0)	<0.001
Socio-economic factors - no/total no, (%)			
Living alone	927/2678 (34.6)	320/1010 (31.7)	0.093
Living in rural area	338/2662 (12.7)	107/1014 (10.6)	0.075
Unemployed	145/2616 (5.5)	46/996 (4.6)	0.27

Educational level			0.46
No education	108/2510 (4.3)	47/963 (4.9)	
Primary education	769/2510 (30.6)	292/963 (30.3)	
Secondary education	1203/2510 (47.9)	441/963 (45.8)	
Tertiary education	430/2510 (17.1)	183/963 (19.0)	
TOAST classification			<0.001
Large artery atherosclerosis	743/2507 (29.6)	106/980 (10.8)	
Small vessel disease	665/2507 (26.5)	83/980 (8.5)	
Cardioembolism	0/2507 (0.0)	562/980 (57.4)	
Other determined cause	166/2507 (6.6)	22/980 (2.2)	
Undetermined	33/2507 (37.2)	207/980 (21.1)	
ABCD2 score			0.060
0-3	805/2423 (33.2)	275/915 (30.0)	
4-5	1131/2423 (46.7)	469/915 (51.3)	
6-7	487/2423 (20.1)	171/915 (18.7)	
Acute infarction			0.001
No	1419/2602 (54.5)	492/1012 (48.6)	
Single	784/2602 (30.1)	323/1012 (31.9)	
Multiple	399/2602 (15.3)	197/1012 (19.5)	
PICO's score			0.16
0	1792/2733 (64.6)	685/1026 (66.8)	
1	762/2733 (27.9)	291/1026 (28.4)	
≥2	179/2733 (6.5)	50/1026 (4.9)	

eTable 16. Multivariable Association Between Baseline Characteristics and ASCOD Grades C1-C2 and C3 vs C0

	OR (95%CI)	P-value
Atrial fibrillation or flutter	18.1 (13.1-25.0)	<0.001
Ethnicity		
Non-Asian	1.00 (ref.)	-
Asian	0.49 (0.40-0.61)	<0.001
Qualifying event		
TIA	1.00 (ref.)	-
Stroke	1.53 (1.30-1.81)	<0.001
Clinically significant valvular disease or prosthetic heart valve	2.56 (1.57-4.18)	<0.001
Congestive heart failure	2.40 (1.48-3.89)	<0.001
Coronary artery disease	1.52 (1.19-1.94)	0.001
Systolic, per 24 mm Hg increase	0.86 (0.79-0.94)	0.001
Triglycerides, per 86 mg/dL increase	0.83 (0.74-0.93	0.002
Living alone	0.81 (0.68-0.96)	0.017
Diabetes	0.77 (0.61-0.96)	0.021
Living in rural area	0.74 (0.57-0.97)	0.027
LDL, per 40 mg/dL increase	0.91 (0.83-0.99)	0.043

eTable 17. Univariate Comparison Between Baseline Characteristics and ASCOD Grades C1-C2 vs A0, S0, C0, O0, and D0

	A0/S0/C0/OD0 (n=484)	C1/C2 (n=800)	P-value
Age-yr, mean (SD)	58.4 (14.7)	70.2 (12.4)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	477/800 (59.6)	0.007
Ethnicity			0.43
Asian	80/484 (16.5)	146/800 (18.3)	
Non-Asian	404/484 (83.5)	654/800 (81.7)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	388/787 (49.3)	
TIA	326/432 (75.5)	399/787 (50.7)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	638/798 (80.0)	<0.001
Diabetes	59/480 (12.3)	142/797 (17.8)	0.009
Dyslipidemia	287/448 (59.3)	551/800 (68.9)	0.001
Smoke - no/total no, (%)			<0.001
Never	273/475 (57.5)	459/791 (58.0)	
Former	93/475 (19.6)	213/791 (26.9)	
Current	109/475 (22.9)	119/791 (15.1)	
Regular alcohol consumption	75/477 (15.7)	169/789 (21.4)	0.013
Regular physical activity	148/467 (31.7)	148/780 (19.0)	<0.001
Stroke or TIA	46/484 (9.5)	148/800 (18.5)	<0.001
Coronary artery disease	0/480 (0.0)	185/796 (23.2)	<0.001
Peripheral artery disease	0/474 (0.0)	35/795 (4.4)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	281/794 (35.4)	<0.001
Congestive heart failure	0/482 (0.0)	65/795 (8.2)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	67/800 (8.4)	<0.001
Atherogenic dyslipidemia[1]	28/349 (8.0)	42/653 (6.4)	0.35
Atherogenic dyslipidemia[2]	67/349 (19.2)	119/653 (18.2)	0.71
Diabetes and Atherogenic dyslipidemia[2]	15/482 (3.1)	40/800 (5.0)	0.11
Body-mass index, mean (SD)	26.4 (4.7)	26.4 (4.6)	0.93
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	144 (25)	0.005
Diastolic, mean (SD)	81 (12)	79 (15)	0.18
Glucose-mg/dl, median (IQR)	99 (90-121)	104 (90-126)	0.58
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	112 (38)	<0.001
HDL, mean (SD)	53 (19)	50 (15)	0.015
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	110.0 (83.0-156.0)	0.27
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	248/791 (31.4)	0.89
Living in rural area	51/465 (11.0)	97/792 (12.3)	0.50
Unemployed	35/459 (7.6)	38/777 (4.9)	0.049

Educational level			0.002
No education	14/434 (3.2)	44/748 (5.9)	
Primary education	113/434 (26.0)	245/748 (32.8)	
Secondary education	206/434 (47.5)	337/748 (45.0)	
Tertiary education	101/424 (23.3)	122/748 (16.3)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	68/760 (8.9)	
Small vessel disease	0/395 (0.0)	40/760 (5.3)	
Cardioembolism	0/395 (0.0)	562/760 (73.9)	
Other determined cause	0/395 (0.0)	8/760 (1.1)	
Undetermined	341/395 (86.3)	82/760 (10.8)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	183/704 (26.0)	
4-5	164/418 (39.2)	381/704 (54.1)	
6-7	46/418 (11.0)	140/704 (19.9)	
Acute infarction			<0.001
No	322/432 (74.5)	371/787 (47.2)	
Single	81/432 (18.8)	245/787 (31.1)	
Multiple	29/432 (6.7)	171/787 (21.7)	
PICO's score			<0.001
0	484/484 (100.0)	526/800 (65.8)	
1	0/484 (0.0)	241/800 (30.1)	
≥2	0/484 (0.0)	33/800 (4.1)	

eTable 18. Univariate Comparison Between Baseline Characteristics and ASCOD Grades C1-C2 and C3 vs A0, S0, C0, O0, and D0

	A0/S0/C0/OD0 (n=484)	C1/C2/C3 (n=1026)	P-value
Age-yr, mean (SD)	58.4 (14.7)	68.3 (13.5)	<0.001
Male sex - no/total no, (%)	250/482 (51.9)	615/1026 (59.9)	0.003
Ethnicity			0.98
Asian	80/484 (16.5)	169/1026 (16.5)	
Non-Asian	404/484 (83.5)	857/1026 (83.5)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	582/1012 (47.6)	
TIA	326/432 (75.5)	530/1012 (52.4)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	765/1024 (74.7)	<0.001
Diabetes	59/480 (12.3)	169/1022 (16.5)	0.033
Dyslipidemia	287/448 (59.3)	706/1026 (68.8)	<0.001
Smoke - no/total no, (%)			0.002
Never	273/475 (57.5)	577/1014 (56.9)	
Former	93/475 (19.6)	267/1014 (26.3)	
Current	109/475 (22.9)	170/1014 (16.8)	
Regular alcohol consumption	75/477 (15.7)	220/1014 (21.7)	0.007
Regular physical activity	148/467 (31.7)	217/1000 (21.7)	<0.001
Stroke or TIA	46/484 (9.5)	179/1026 (17.5)	<0.001
Coronary artery disease	0/480 (0.0)	198/1021 (19.4)	<0.001
Peripheral artery disease	0/474 (0.0)	38/1018 (3.7)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	284/1020 (27.8)	<0.001
Congestive heart failure	0/482 (0.0)	69/1021 (6.8)	<0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	67/1026 (6.5)	<0.001
Atherogenic dyslipidemia[1]	28/349 (8.0)	54/858 (6.3)	0.28
Atherogenic dyslipidemia[2]	67/349 (19.2)	146/858	0.37
Diabetes and Atherogenic dyslipidemia[2]	15/482 (3.1)	47/1026 (4.6)	0.18
Body-mass index, mean (SD)	26.4 (4.7)	26.3 (4.5)	0.71
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	143 (24)	0.006
Diastolic, mean (SD)	81 (12)	80 (15)	0.20
Glucose-mg/dl, median (IQR)	99 (90-121)	103 (90-124)	0.81
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	114 (38)	<0.001
HDL, mean (SD)	53 (19)	51 (16)	0.087
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	109.0 (82.0-151.0)	0.14
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	320/1010 (31.7)	0.79
Living in rural area	51/465 (11.0)	107/1014 (10.6)	0.81
Unemployed	35/459 (7.6)	46/996 (4.6)	0.020

Educational level			0.085
No education	14/434 (3.2)	47/963 (4.9)	
Primary education	113/434 (26.0)	292/963 (30.3)	
Secondary education	206/434 (47.5)	441/963 (45.8)	
Tertiary education	101/424 (23.3)	183/963 (19.0)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	106/980 (10.8)	
Small vessel disease	0/395 (0.0)	83/980 (8.5)	
Cardioembolism	0/395 (0.0)	562/980 (57.4)	
Other determined cause	0/395 (0.0)	22/980 (2.2)	
Undetermined	341/395 (86.3)	207/980 (21.1)	
ABCD2 score			<0.001
0-3	208/418 (49.8)	275/915 (30.0)	
4-5	164/418 (39.2)	469/915 (51.3)	
6-7	46/418 (11.0)	171/915 (18.7)	
Acute infarction			<0.001
No	322/432 (74.5)	492/1012 (48.6)	
Single	81/432 (18.8)	323/1012 (31.9)	
Multiple	29/432 (6.7)	197/1012 (19.5)	
PICO's score			<0.001
0	484/484 (100.0)	685/1026 (66.7)	
1	0/484 (0.0)	291/1026 (28.4)	
≥2	0/484 (0.0)	50/1026 (4.9)	

eTable 19. Baseline Characteristics According to ASCOD Grading System OD (Other Cause and Dissection)

	O0/D0 (n=3392)	O1/D1 or O2/D2 (n=206)	O3/D3 (n=249)
Age-yr, mean (SD)	67.1 (13.1)	61.5 (14.1)	61.4 (12.4)
Male sex - no/total no, (%)	1403/3388 (41.4)	95/206 (46.1)	48/247 (19.4)
Ethnicity			
Asian	757/3392 (22.3)	36/206 (17.5)	89/249 (35.7)
Non-Asian	2635/3392 (77.7)	170/206 (82.5)	160/249 (64.3)
Qualifying event			
Stroke	1419/3287 (43.2)	63/202 (31.2)	106/205 (51.7)
TIA	1868/3287 (56.8)	139/202 (68.8)	99/205 (48.3)
Medical history - no/total no, (%)			
Hypertension	2415/3385 (71.3)	125/206 (60.7)	167/246 (67.9)
Diabetes	661/3378 (19.6)	26/206 (12.6)	40/248 (16.1)
Dyslipidemia	2434/3392 (71.8)	115/206 (55.8)	160/249 (64.3)
Smoke - no/total no, (%)			
Never	1812/3349 (54.1)	105/205 (51.2)	107/247 (43.3)
Former	825/3349 (24.6)	58/205 (28.3)	59/247 (23.9)
Current	712/3349 (21.3)	42/205 (20.5)	81/247 (32.8)
Regular alcohol consumption	684/3350 (20.4)	48/205 (23.4)	66/246 (26.8)
Regular physical activity	706/3301 (21.4)	61/203 (30.1)	34/208 (16.4)
Stroke or TIA	587/3392 (17.3)	32/206 (15.5)	39/249 (15.7)
Coronary artery disease	438/3380 (13.0)	17/204 (8.3)	26/249 (10.4)
Peripheral artery disease	103/3369 (3.1)	7/203 (3.5)	3/247 (1.2)
Atrial fibrillation or flutter	304/3382 (9.0)	10/205 (4.9)	21/249 (8.4)
Congestive heart failure	99/3382 (2.9)	4/205 (2.0)	6/249 (2.4)
Clinically significant valvular disease or prosthetic heart valve	96/3392 (2.8)	4/206 (1.9)	5/249 (2.0)
Atherogenic dyslipidemia[1]	238/2725 (8.7)	19/191 (10.0)	15/175 (8.6)

Atherogenic dyslipidemia([2])	561/2726 (20.6)	48/191 (25.1)	46/176 (26.1)
Diabetes and Atherogenic dyslipidemia([2])	176/3386 (5.2)	8/206 (3.9)	13/248 (5.2)
Body-mass index, mean (SD)	26.3 (4.5)	26.6 (5.1)	27.2 (5.1)
Blood pressure-mm Hg			
Systolic, mean (SD)	146 (24)	138 (51)	150 (24)
Diastolic, mean (SD)	81 (13)	80 (13)	86 (15)
Glucose-mg/dl, median (IQR)	103 (90-128)	108 (92-167)	103 (90-126)
Cholesterol- mg/dl			
LDL, mean (SD)	118 (41)	122 (38)	129 (42)
HDL, mean (SD)	51 (16)	52 (16)	46 (12)
Triglyceride, median(IQR), mg/dl	115.0 (87.0-162.0)	133.0 (91.0-188.0)	135.0 (106.0-171.0)
Socio-economic factors - no/total no, (%)			
Living alone	1141/3334 (34.2)	61/206 (29.6)	66/233 (28.3)
Living in rural area	356/3347 (10.6)	65/206 (31.6)	33/210 (15.7)
Unemployed	165/3286 (5.0)	13/206 (6.3)	17/206 (8.3)
Educational level			
No education	147/3159 (4.6)	3/199 (1.5)	9/198 (4.5)
Primary education	988/3159 (31.3)	42/199 (21.1)	50/198 (25.3)
Secondary education	1482/3159 (46.9)	114/199 (57.3)	101/198 (51.0)
Tertiary education	542/3159 (17.2)	40/199 (20.1)	38/198 (19.2)
TOAST classification			
Large artery atherosclerosis	807/3151 (25.6)	1/203 (0.5)	68/204 (33.3)
Small vessel disease	718/3151 (22.8)	4/203 (2.0)	40/204 (19.6)
Cardioembolism	525/3151 (16.7)	0/203 (0.0)	37/204 (18.1)
Other determined cause	0/3151 (0.0)	196/206 (96.5)	0/204 (0.0)
Undetermined	1101/3151 (34.9)	2/203 (1.0)	59/204 (28.9)
ABCD2 score			
0-3	935/3033 (30.8)	104/192 (54.2)	64/192 (33.3)

4-5	1476/3033 (48.7)	67/192 (34.9)	98/192 (51.1)
6-7	622/3033 (20.5)	21/192 (10.9)	30/192 (15.6)
Acute infarction			
No	1735/3287 (52.8)	132/202 (65.3)	97/205 (47.3)
Single	1011/3287 (30.8)	46/202 (22.8)	68/205 (33.2)
Multiple	541/3287 (16.4)	24/202 (11.9)	40/205 (19.5)
PICO's score			
0	2189/3392 (64.5)	161/206 (78.2)	204/249 (81.9)
1	987/3392 (29.1)	35/260 (17.0)	39/249 (15.7)
≥2	216/3392 (6.4)	10/206 (4.8)	6/249 (2.4)
Score at discharge			
NIHSS at discharge			
0	2476/3091 (80.1)	167/191 (87.4)	147/194 (75.8)
1-4	598/3091 (19.4)	22/191 (11.5)	44/194 (22.7)
>5	17/3091 (0.5)	2/191 (1.1)	3/194 (1.6)
RANKIN at discharge >1 - no/total no, (%)	60/3123 (1.9)	2/187 (1.1)	7/195 (3.6)

[1] Define as triglycerides >200 mg/dL and HDL ≤40 mg/dL for men (HDL ≤50 mg/dL for women);

[2] Define as triglycerides >150 mg/dL an HDL ≤50 mg/dL

eTable 20. Five-Year Event Rates According to ASCOD Grades (Other Causes and Dissection)

	O0/D0 (n=3392)	O1/D1 or O2/D2 (n=206)	O3/D3 (n=249)	P-value[1]	P-value[2]
Major cardiovascular event	411 (12.9)	26 (13.6)	32 (13.4)	0.92[a]	0.75 [a]
Recurrent stroke	300 (9.3)	22 (11.5)	23 (9.6)	0.63 [a]	0.34 [a]
Death	343 (11.1)	10 (5.4)	20 (8.5)	0.038[b]	0.020 [b]

Values are number of events (event rate expressed as % estimated from Kaplan-Meier or Kalbfleisch and Prentice estimates for time to event outcomes).

[1] P-value for comparing the three groups; [2] P-value for comparing O0/D0 vs. O1/D1

P-value were calculated using Gray's test ([a]) or log-rank test ([b])

eTable 21. Effect Sizes Associated With ASCOD Grades O1-D1 or O2-D2 and O3-O3 Compared With O0-D0

	O0/D0	O1/D1 or O2/D2		O3/D3	
		HR (95% CI)	P	HR (95% CI)	P
Major cardiovascular event	1.00 (reference)	1.07 (0.72-1.58)	0.75	1.05 (0.73-1.51)	0.79
Recurrent stroke	1.00 (reference)	1.24 (0.80-1.90)	0.34	1.04 (0.68-1.58)	0.87
Death	1.00 (reference)	0.48 (0.26-0.90)	0.020	0.77 (0.49-1.20)	0.25

Abbreviations: CI=confidence interval; HR=hazard ratio

eTable 22. Univariate Comparison Between Baseline Characteristics and ASCOD Grades O1-1 or O2-D2 vs O0-D0

	O0/D0 (n=3392)	O1/D1 or O2/D2 (n=206)	P-value
Age-yr, mean (SD)	67.1 (13.1)	61.5 (14.1)	<0.001
Male sex - no/total no, (%)	1403/3388 (41.4)	95/206 (46.1)	0.19
Ethnicity			0.12
Asian	757/3392 (22.3)	36/206 (17.5)	
Non-Asian	2635/3392 (77.7)	170/206 (82.5)	
Qualifying event			0.001
Stroke	1419/3287 (43.2)	63/202 (31.2)	
TIA	1868/3287 (56.8)	139/202 (68.8)	
Medical history - no/total no, (%)			
Hypertension	2415/3385 (71.3)	125/206 (60.7)	0.001
Diabetes	661/3378 (19.6)	26/206 (12.6)	0.014
Dyslipidemia	2434/3392 (71.8)	115/206 (55.8)	<0.001
Smoke - no/total no, (%)			0.50
Never	1812/3349 (54.1)	105/205 (51.2)	
Former	825/3349 (24.6)	58/205 (28.3)	
Current	712/3349 (21.3)	42/205 (20.5)	
Regular alcohol consumption	684/3350 (20.4)	48/205 (23.4)	0.30
Regular physical activity	706/3301 (21.4)	61/203 (30.1)	0.004
Stroke or TIA	587/3392 (17.3)	32/206 (15.5)	0.51
Coronary artery disease	438/3380 (13.0)	17/204 (8.3)	0.054
Peripheral artery disease	103/3369 (3.1)	7/203 (3.5)	0.75
Atrial fibrillation or flutter	304/3382 (9.0)	10/205 (4.9)	0.043
Congestive heart failure	99/3382 (2.9)	4/205 (2.0)	0.42
Clinically significant valvular disease or prosthetic heart valve	96/3392 (2.8)	4/206 (1.9)	0.45
Atherogenic dyslipidemia[1]	238/2725 (8.7)	19/191 (10.0)	0.57

Atherogenic dyslipidemia([2])	561/2726 (20.6)	48/191 (25.1)	0.13
Diabetes and Atherogenic dyslipidemia([2])	176/3386 (5.2)	8/206 (3.9)	0.41
Body-mass index, mean (SD)	26.3 (4.5)	26.6 (5.1)	0.30
Blood pressure-mm Hg			
Systolic, mean (SD)	146 (24)	138 (51)	<0.001
Diastolic, mean (SD)	81 (13)	80 (13)	0.24
Glucose-mg/dl, median (IQR)	103 (90-128)	108 (92-167)	0.001
Cholesterol- mg/dl			
LDL, mean (SD)	118 (41)	122 (38)	0.20
HDL, mean (SD)	51 (16)	52 (16)	0.44
Triglyceride, median(IQR), mg/dl	115.0 (87.0-162.0)	133.0 (91.0-188.0)	0.005
Socio-economic factors - no/total no, (%)			
Living alone	1141/3334 (34.2)	61/206 (29.6)	0.18
Living in rural area	356/3347 (10.6)	65/206 (31.6)	<0.001
Unemployed	165/3286 (5.0)	13/206 (6.3)	0.41
Educational level			0.001
No education	147/3159 (4.6)	3/199 (1.5)	
Primary education	988/3159 (31.3)	42/199 (21.1)	
Secondary education	1482/3159 (46.9)	114/199 (57.3)	
Tertiary education	542/3159 (17.2)	40/199 (20.1)	
TOAST classification			<0.001
Large artery atherosclerosis	807/3151 (25.6)	1/203 (0.5)	
Small vessel disease	718/3151 (22.8)	4/203 (2.0)	
Cardioembolism	525/3151 (16.7)	0/203 (0.0)	
Other determined cause	0/3151 (0.0)	196/206 (96.5)	
Undetermined	1101/3151 (34.9)	2/203 (1.0)	
ABCD2 score			<0.001
0-3	935/3033 (30.8)	104/192 (54.2)	

4-5	1476/3033 (48.7)	67/192 (34.9)	
6-7	622/3033 (20.5)	21/192 (10.9)	
Acute infarction			0.002
No	1735/3287 (52.8)	132/202 (65.3)	
Single	1011/3287 (30.8)	46/202 (22.8)	
Multiple	541/3287 (16.4)	24/202 (11.9)	
PICO's score			<0.001
0	2189/3392 (64.5)	161/206 (78.2)	
1	987/3392 (29.1)	35/260 (17.0)	
≥2	216/3392 (6.4)	10/206 (4.8)	

eTable 23. Multivariable Association Between Baseline Characteristics and ASCOD Grades O1-D1 or O2-D2 vs ASCOD Grade O0-D0

	OR (95%CI)	P-value
Living in rural area	3.52 (2.55-4.87)	<0.001
ABCD2 score		
0-3	1.00 (ref.)	-
4-5	0.56 (0.40-0.79)	0.001
6-7	0.53 (0.31-0.90)	0.019
Dyslipidemia	0.62 (0.46-0.84)	0.002
Age, per 10 years increase	0.86 (0.77-0.96)	0.006
Triglycerides, per 86 mg/dL increase	1.17 (1.03-1.32)	0.012
Systolic, per 24 mm Hg increase	0.82 (0.69-0.98)	0.025

eTable 24. Univariate Comparison Between Baseline Characteristics and ASCOD Grades O1-D1 or O2-D2 or O3-D3 vs O0-D0

	O0/D0 (n=3392)	O1/D1 or O2/D2 or O0/D3 (n=455)	P-value
Age-yr, mean (SD)	67.1 (13.1)	61.5 (13.2)	<0.001
Male sex - no/total no, (%)	1403/3388 (41.4)	143/453 (31.6)	<0.001
Ethnicity			0.014
Asian	757/3392 (22.3)	125/455 (27.5)	
Non-Asian	2635/3392 (77.7)	330/455 (72.5)	
Qualifying event			0.53
Stroke	1419/3287 (43.2)	169/407 (41.5)	
TIA	1868/3287 (56.8)	238/407 (58.5)	
Medical history - no/total no, (%)			
Hypertension	2415/3385 (71.3)	292/452 (64.6)	0.003
Diabetes	661/3378 (19.6)	66/454 (14.5)	0.010
Dyslipidemia	2434/3392 (71.8)	275/455 (60.4)	<0.001
Smoke - no/total no, (%)			0.005
Never	1812/3349 (54.1)	212/452 (46.9)	
Former	825/3349 (24.6)	117/452 (25.9)	
Current	712/3349 (21.3)	123/452 (27.2)	
Regular alcohol consumption	684/3350 (20.4)	114/451 (25.3)	0.017
Regular physical activity	706/3301 (21.4)	95/411 (23.1)	0.42
Stroke or TIA	587/3392 (17.3)	71/455 (15.6)	0.37
Coronary artery disease	438/3380 (13.0)	43/453 (9.5)	0.037
Peripheral artery disease	103/3369 (3.1)	10/450 (2.2)	0.33
Atrial fibrillation or flutter	304/3382 (9.0)	31/454 (6.8)	0.13
Congestive heart failure	99/3382 (2.9)	10/454 (2.2)	0.38
Clinically significant valvular disease or prosthetic heart valve	96/3392 (2.8)	9/455 (2.0)	0.29
Atherogenic dyslipidemia[1]	238/2725 (8.7)	34/366 (9.3)	0.72
Atherogenic dyslipidemia[2]	561/2726 (20.6)	94/367 (25.6)	0.037
Diabetes and Atherogenic dyslipidemia[2]	176/3386 (5.2)	21/454 (4.6)	0.60
Body-mass index, mean (SD)	26.3 (4.5)	26.9 (5.1)	0.010
Blood pressure-mm Hg			
Systolic, mean (SD)	146 (24)	145 (23)	0.19
Diastolic, mean (SD)	81 (13)	83 (14)	0.002
Glucose-mg/dl, median (IQR)	103 (90-128)	104 (92-135)	0.042
Cholesterol- mg/dl			
LDL, mean (SD)	118 (41)	125 (40)	0.003
HDL, mean (SD)	51 (16)	49 (14)	0.039
Triglyceride, median(IQR), mg/dl	115.0 (87.0-162.0)	135.0 (97.0-180.0)	<0.001

Socio-economic factors - no/total no, (%)

Living alone	1141/3334 (34.2)	127/439 (28.9)	0.027
Living in rural area	356/3347 (10.6)	98/416 (23.6)	<0.001
Unemployed	165/3286 (5.0)	30/412 (7.3)	0.053
Educational level			0.002
No education	147/3159 (4.6)	12/397 (3.0)	
Primary education	988/3159 (31.3)	92/397 (23.2)	
Secondary education	1482/3159 (46.9)	215/397 (54.2)	
Tertiary education	542/3159 (17.2)	78/397 (19.6)	
TOAST classification			<0.001
Large artery atherosclerosis	807/3151 (25.6)	69/407 (16.9)	
Small vessel disease	718/3151 (22.8)	44/107 (10.8)	
Cardioembolism	525/3151 (16.7)	37/407 (9.1)	
Other determined cause	0/3151 (0.0)	196/407 (48.2)	
Undetermined	1101/3151 (34.9)	61/407 (15.0)	
ABCD2 score			<0.001
0-3	935/3033 (30.8)	168/384 (43.7)	
4-5	1476/3033 (48.7)	165/384 (43.0)	
6-7	622/3033 (20.5)	51/384 (13.3)	
Acute infarction			0.40
No	1735/3287 (52.8)	229/407 (56.3)	
Single	1011/3287 (30.8)	114/407 (28.0)	
Multiple	541/3287 (16.4)	64/407 (15.7)	
PICO's score			<0.001
0	2189/3392 (64.5)	365/455 (80.2)	
1	987/3392 (29.1)	74/455 (16.3)	
≥2	216/3392 (6.4)	16/455 (3.5)	

eTable 25. Multivariable Association Between Baseline Characteristics and ASCOD Grades O1-D1 or O2-D2 or O3-D3 vs O0-D0

	OR (95%CI)	P-value
Living in rural area	2.55 (1.95-3.32)	<0.001
Age, per 10 years increase	0.85 (0.78-0.93)	<0.001
PICO's score		
0	1.00 (ref.)	-
1	0.60 (0.46-0.80)	<0.001
≥2	0.62 (0.37-1.07)	0.084
Male sex	1.48 (1.19-1.85)	0.001
Dyslipidemia	0.69 (0.55-0.85)	0.001
Ethnicity		
Non-Asian	1.00 (ref.)	-
Asian	1.47 (1.16-1.86)	0.002
ABCD2 score		
0-3	1.00 (ref.)	-
4-5	0.75 (0.59-0.95)	0.020
6-7	0.61 (0.43-0.87)	0.006
Triglycerides, per 86 mg/dL increase	1.12 (1.02-1.23)	0.016
LDL, per 40 mg/dL increase	1.13 (1.02-1.26)	0.022
Diastolic, per 13 mm Hg increase	1.12 (1.01-1.25)	0.029

eTable 26. Univariate Comparison Between Baseline Characteristics and ASCOD Grades O1-D1 or O2-D2 vs A0, S0, C0, O0, and D0

	A0/S0/C0/OD0 (n=484)	O1/D1 or O2/D2 (n=206)	P-value
Age-yr, mean (SD)	58.4 (14.7)	61.5 (14.1)	0.012
Male sex - no/total no, (%)	250/482 (51.9)	95/206 (46.1)	0.63
Ethnicity			0.76
Asian	80/484 (16.5)	36/206 (17.5)	
Non-Asian	404/484 (83.5)	170/206 (82.5)	
Qualifying event			0.078
Stroke	106/432 (24.5)	63/202 (31.2)	
TIA	326/432 (75.5)	139/202 (68.8)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	125/206 (60.7)	0.010
Diabetes	59/480 (12.3)	26/206 (12.6)	0.90
Dyslipidemia	287/448 (59.3)	115/206 (55.8)	0.40
Smoke - no/total no, (%)			0.043
Never	273/475 (57.5)	105/205 (51.2)	
Former	93/475 (19.6)	58/205 (28.3)	
Current	109/475 (22.9)	42/205 (20.5)	
Regular alcohol consumption	75/477 (15.7)	48/205 (23.4)	0.017
Regular physical activity	148/467 (31.7)	61/203 (30.1)	0.67
Stroke or TIA	46/484 (9.5)	32/206 (15.5)	0.022
Coronary artery disease	0/480 (0.0)	17/204 (8.3)	<0.001
Peripheral artery disease	0/474 (0.0)	7/203 (3.5)	<0.001
Atrial fibrillation or flutter	4/482 (0.8)	10/205 (4.9)	0.001
Congestive heart failure	0/482 (0.0)	4/205 (2.0)	0.008
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	4/206 (1.9)	0.21
Atherogenic dyslipidemia([1])	28/349 (8.0)	19/191 (10.0)	0.45
Atherogenic dyslipidemia([2])	67/349 (19.2)	48/191 (25.1)	0.11
Diabetes and Atherogenic dyslipidemia([2])	15/482 (3.1)	8/206 (3.9)	0.61
Body-mass index, mean (SD)	26.4 (4.7)	26.6 (5.1)	0.60
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	138 (51)	0.52
Diastolic, mean (SD)	81 (12)	80 (13)	0.41
Glucose-mg/dl, median (IQR)	99 (90-121)	108 (92-167)	0.001
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	122 (38)	0.49
HDL, mean (SD)	53 (19)	52 (16)	0.42
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	133.0 (91.0-188.0)	0.007
Socio-economic factors - no/total no, (%)			
Living alone	145/468 (31.0)	61/206 (29.6)	0.72
Living in rural area	51/465 (11.0)	65/206 (31.6)	<0.001

Unemployed	35/459 (7.6)	13/206 (6.3)	0.54
Educational level			0.11
No education	14/434 (3.2)	3/199 (1.5)	
Primary education	113/434 (26.0)	42/199 (21.1)	
Secondary education	206/434 (47.5)	114/199 (57.3)	
Tertiary education	101/424 (23.3)	40/199 (20.1)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	1/203 (0.5)	
Small vessel disease	0/395 (0.0)	4/203 (2.0)	
Cardioembolism	0/395 (0.0)	0/203 (0.0)	
Other determined cause	0/395 (0.0)	196/206 (96.5)	
Undetermined	341/395 (86.3)	2/203 (1.0)	
ABCD2 score			0.56
0-3	208/418 (49.8)	104/192 (54.2)	
4-5	164/418 (39.2)	67/192 (34.9)	
6-7	46/418 (11.0)	21/192 (10.9)	
Acute infarction			0.028
No	322/432 (74.5)	132/202 (65.3)	
Single	81/432 (18.8)	46/202 (22.8)	
Multiple	29/432 (6.7)	24/202 (11.9)	
PICO's score			<0.001
0	484/484 (100.0)	161/206 (78.2)	
1	0/484 (0.0)	35/206 (17.0)	
≥2	0/484 (0.0)	10/206 (4.8)	

eTable 27. Univariate Comparison Between Baseline Characteristics and ASCOD Grades O1-D1 or O2-D2 or O3-D3 vs A0, S0, C0, O0, or D0

	A0/S0/C0/OD0 (n=484)	O1/D1 or O2/D2 or O0/D3 (n=455)	P-value
Age-yr, mean (SD)	58.4 (14.7)	61.5 (13.2)	0.001
Male sex - no/total no, (%)	250/482 (51.9)	143/453 (31.6)	<0.001
Ethnicity			<0.001
Asian	80/484 (16.5)	125/455 (27.5)	
Non-Asian	404/484 (83.5)	330/455 (72.5)	
Qualifying event			<0.001
Stroke	106/432 (24.5)	169/407 (41.5)	
TIA	326/432 (75.5)	238/407 (58.5)	
Medical history - no/total no, (%)			
Hypertension	240/481 (49.9)	292/452 (64.6)	<0.001
Diabetes	59/480 (12.3)	66/454 (14.5)	0.31
Dyslipidemia	287/448 (59.3)	275/455 (60.4)	0.72
Smoke - no/total no, (%)			0.005
Never	273/475 (57.5)	212/452 (46.9)	
Former	93/475 (19.6)	117/452 (25.9)	
Current	109/475 (22.9)	123/452 (27.2)	
Regular alcohol consumption	75/477 (15.7)	114/451 (25.3)	<0.001
Regular physical activity	148/467 (31.7)	95/411 (23.1)	0.005
Stroke or TIA	46/484 (9.5)	71/455 (15.6)	0.005
Coronary artery disease	0/480 (0.0)	43/453 (9.5)	<0.001
Peripheral artery disease	0/474 (0.0)	10/450 (2.2)	0.001
Atrial fibrillation or flutter	4/482 (0.8)	31/454 (6.8)	<0.001
Congestive heart failure	0/482 (0.0)	10/454 (2.2)	0.001
Clinically significant valvular disease or prosthetic heart valve	3/484 (0.6)	9/455 (2.0)	0.064
Atherogenic dyslipidemia[1]	28/349 (8.0)	34/366 (9.3)	0.55
Atherogenic dyslipidemia[2]	67/349 (19.2)	94/367 (25.6)	0.040
Diabetes and Atherogenic dyslipidemia[2]	15/482 (3.1)	21/454 (4.6)	0.23
Body-mass index, mean (SD)	26.4 (4.7)	26.9 (5.1)	0.14
Blood pressure-mm Hg			
Systolic, mean (SD)	140 (22)	145 (23)	0.001
Diastolic, mean (SD)	81 (12)	83 (14)	0.005
Glucose-mg/dl, median (IQR)	99 (90-121)	104 (92-135)	0.027
Cholesterol- mg/dl			
LDL, mean (SD)	125 (42)	125 (40)	0.89
HDL, mean (SD)	53 (19)	49 (14)	0.002
Triglyceride, median(IQR), mg/dl	115.0 (82.0-161.0)	135.0 (97.0-180.0)	<0.001
Socio-economic factors - no/total no, (%)			

Living alone	145/468 (31.0)	127/439 (28.9)	0.50
Living in rural area	51/465 (11.0)	98/416 (23.6)	<0.001
Unemployed	35/459 (7.6)	30/412 (7.3)	0.85
Educational level			0.28
No education	14/434 (3.2)	12/397 (3.0)	
Primary education	113/434 (26.0)	92/397 (23.2)	
Secondary education	206/434 (47.5)	215/397 (54.2)	
Tertiary education	101/424 (23.3)	78/397 (19.6)	
TOAST classification			<0.001
Large artery atherosclerosis	54/395 (13.7)	69/407 (16.9)	
Small vessel disease	0/395 (0.0)	44/107 (10.8)	
Cardioembolism	0/395 (0.0)	37/407 (9.1)	
Other determined cause	0/395 (0.0)	196/407 (48.2)	
Undetermined	341/395 (86.3)	61/407 (15.0)	
ABCD2 score			0.21
0-3	208/418 (49.8)	168/384 (43.7)	
4-5	164/418 (39.2)	165/384 (43.0)	
6-7	46/418 (11.0)	51/384 (13.3)	
Acute infarction			<0.001
No	322/432 (74.5)	229/407 (56.3)	
Single	81/432 (18.8)	114/407 (28.0)	
Multiple	29/432 (6.7)	64/407 (15.7)	
PICO's score			<0.001
0	484/484 (100.0)	365/455 (80.2)	
1	0/484 (0.0)	74/455 (16.3)	
≥2	0/484 (0.0)	16/455 (3.5)	

eTable 28. Five-Year Event Rates and Effect Sizes According to ASCOD Cross-Grades

	A0/S0/C0/O0/D0 (n=484)	A0 (n=1406)	A1/A2 (n=998)	A1/A2/A3 (n=2106)
Major cardiovascular event		101 (7.7; 6.3 to 9.2)	189 (19.8; 17.4 to 22.4)	144 (13.8; 11.8 to 16.0)
S0		55/897 (6.5; 5.0 to 8.3)	95/504 (19.6; 16.2 to 23.2)	162/1065 (15.9; 13.7 to 18.2)
SHR (95% CI)		-	4.81 (2.97-7.80)***	3.84 (2.41-6.11)***
S1/S2		29/323 (9.6; 6.6 to 13.3)	16/110 (16.1; 9.6 to 24.1)	46/380 (13.1; 9.8 to 16.8)
SHR (95% CI)		2.21 (1.25-3.90)**	3.71 (1.93-7.13)***	3.06 (1.81-5.17)***
S1/S2/S3	20 (4.4)	45/501 (9.7; 7.2 to 12.6)	94/489 (20.3; 16.8 to 24.1)	169/1028 (17.6; 15.2 to 20.1)
SHR (95% CI)	(2.8 to 6.5)	2.20 (1.30-3.72)**	4.96 (3.06-8.05)***	4.23 (2.66-6.74)***
C0		65/1028 (6.8; 5.3 to 8.5)	130/702 (19.4; 16.5 to 22.5)	224/1465 (16.2; 14.3 to 18.2)
SHR (95% CI)		-	4.74 (2.96-7.59)***	3.88 (2.45-6.14)***
C1/C2		22/244 (9.7; 6.3 to 14.0)	52/225 (24.2; 18.7 to 30.2)	94/479 (20.8; 17.1 to 24.6)
SHR (95% CI)		2.23 (1.22-4.09)**	6.07 (3.62-10.17)***	5.14 (3.17-8.34)***
C1/C2/C3		31/340 (9.7; 6.8 to 13.3)	58/275 (22.1; 17.3 to 27.3)	103/597 (18.2; 15.2 to 21.5)
SHR (95% CI)		2.25 (1.28-3.95)**	5.48 (3.30-9.11)***	4.47 (2.77-7.21)***
Recurrent stroke		75 (5.6)	141 (14.7)	108 (10.3)
S0		40/897 (4.7)	76/504 (15.6)	121/1065 (11.8)
SHR (95% CI)		-	6.34 (3.45-11.67)***	4.73 (2.61-8.57)***
S1/S2		23/323 (7.5)	11/110 (11.0)	38/380 (10.8)
SHR (95% CI)		2.92 (1.45-5.87)***	4.18 (1.85-9.45)***	4.18 (2.18-8.02)***
S1/S2/S3		35/501 (7.4)	65/489 (13.9)	126/1028 (13.1)
SHR (95% CI)	12 (2.6)	2.85 (1.48-5.50)***	5.59 (3.02-10.35)***	5.17 (2.86-9.38)***
C0		43/1028 (4.4)	99/702 (14.7)	172/1465 (12.4)
SHR (95% CI)		-	5.93 (3.26-10.81)***	4.91 (2.73-8.83)***
C1/C2		20/244 (8.8)	35/225 (16.2)	63/479 (13.9)
SHR (95% CI)		3.39 (1.66-6.95)***	6.58 (3.41-12.69)***	5.57 (3.00-10.35)***
C1/C2/C3		29/340 (9.0)	41/275 (15.5)	72/597 (12.7)

SHR (95% CI)		3.52 (1.90-6.91)***	6.29 (3.30-11.98)***	5.09 (2.76-9.38)***
Death		87 (6.8)	139 (15.0)	106 (10.5)
S0		45/897 (5.5)	57/504 (12.1)	102/1065 (10.4)
HR (95% CI)		-	2.72 (1.63-4.52)***	2.32 (1.44-3.74)**
S1/S2		16/323 (5.4)	16/110 (16.4)	37/380 (11.0)
HR (95% CI)		1.20 (0.62-2.31)	3.67 (1.90-7.08)***	2.41 (1.40-4.16)**
S1/S2/S3		42/501 (9.2)	82/489 (18.2)	143/1028 (15.3)
HR (95% CI)	20 (4.5)	2.05 (1.21-3.50)**	4.23 (2.59-6.89)***	3.51 (2.20-5.61)***
C0		54/1028 (5.8)	83/702 (12.8)	150/1465 (11.2)
HR (95% CI)		-	2.88 (1.77-4.69)***	2.50 (1.57-3.99)***
C1/C2		29/244 (13.3)	47/225 (22.6)	83/479 (19.0)
HR (95% CI)		3.02 (1.71-5.33)***	5.36 (3.18-9.05)***	4.46 (2.74-7.27)***
C1/C2/C3		29/340 (9.5)	52/275 (20.4)	89/597 (16.4)
HR (95% CI)		2.11 (1.19-3.72)*	4.78 (2.86-8.01)***	3.78 (2.33-6.14)***

*** p-value <0.001; ** p-value <0.01; * p-value <0.05

	A0/S0/C0/O0/D0 (n=484)	S0 (n=2141)	S1/S2 (n=773)	S1/S2/S3 (n=912)
Major cardiovascular event		232 (11.4; 10.1 to 12.8)	80 (11.1; 8.9 to 13.6)	234 (14.9; 13.2to 16.7)
C0		144/1440 (10.6; 9.0 to 12.3)	69/673 (10.9; 8.6 to 13.5)	168/1282 (14.0; 12.1 to 16.0)
SHR (95% CI)	20 (4.4)	-	2.54 (1.54-4.18)***	3.29 (2.07-5.24)***
C1/C2	(2.8 to 6.5)	65/502 (13.6; 10.7 to 16.8)	7/42 (20.3; 8.7 to 35.3)	60/295 (21.9; 17.2 to 27.0)
SHR (95% CI)		3.27 (1.98-5.40)***	4.46 (1.92-10.39)***	5.36 (3.23-8.90)***
C1/C2/C3		79/639 (12.9; 10.4 to 15.7)	9/86 (12.3; 6.0 to 21.0)	64/383 (18.1; 14.2 to 22.3)
SHR (95% CI)		3.11 (1.90-5.07)***	2.68 (1.23-5.85)**	4.31 (2.61-7.13)***
Recurrent stroke		172 (8.4)	65 (9.0)	171 (10.8)
C0		105/1440 (7.7)	58/673 (9.1)	125/1282 (10.3)
SHR (95% CI)		-	3.56 (1.91-6.63)***	4.05 (2.23-7.33)***
C1/C2	12 (2.6)	47/502 (9.8)	3/42 (9.1)	40/295 (14.5)
SHR (95% CI)		3.89 (2.06-7.34)***	3.03 (0.87-10.54)	5.76 (3.02-11.00)***
C1/C2/C3		61/639 (9.9)	5/86 (6.9)	44/383 (12.4)
SHR (95% CI)		3.97 (2.13-7.37)***	2.43 (0.86-6.86)	4.83 (2.55-9.16)***
Death		164 (8.4)	62 (8.9)	209 (13.6)
C0		96/1440 (7.3)	54/673 (8.9)	135/1282 (11.5)
HR (95% CI)		-	1.95 (1.17-3.27)*	2.60 (1.63-4.17)***
C1/C2	20 (4.5)	56/502 (12.3)	5/42 (14.7)	68/295 (25.6)
HR (95% CI)		2.80 (1.68-4.66)***	3.15 (1.18-8.40)*	6.18 (3.75-10.18)***
C1/C2/C3		60/639 (10.3)	6/86 (8.3)	71/383 (20.6)
HR (95% CI)		2.32 (1.40-3.84)**	1.76 (0.71-4.38)	4.84 (2.94-7.94)***

*** p-value <0.001; ** p-value <0.01; * p-value <0.05

eTable 29. Multivariable Association Between Baseline Characteristics and ASCOD Grades A1-A2 and A1-A2 and A3 vs A0, S0, C0, O0, or D0

	A1/A2 OR (95%CI)	P-value	A1/A2/A3 OR (95%CI)	P-value
Age, per 10 years increase	1.66 (1.47-1.86)	<0.001	1.73 (1.57-1.91)	<0.001
Acute infarction				
No	1.00 (ref.)	-	1.00 (ref.)	-
Single	1.92 (1.39-2.66)	<0.001	2.01 (1.51-2.67)	<0.001
Multiple	3.58 (2.25-5.69)	<0.001	2.78 (1.82-4.24)	<0.001
Hypertension	2.22 (1.64-3.00)	<0.001	1.99 (1.55-2.55)	<0.001
Dyslipidemia	2.01 (1.49-2.71)	<0.001	1.62 (1.27-2.07)	<0.001
Smoke				
Never	1.00 (ref.)	-	1.00 (ref.)	-
Former	1.59 (1.13-2.24)	0.008	1.55 (1.15-2.10)	0.004
Current	2.16 (1.51-3.11)	<0.001	2.10 (1.54-2.86)	<0.001
Regular physical activity	0.55 (0.40-0.75)	<0.001	0.57 (0.43-0.74)	<0.001
Atrial fibrillation or flutter	6.67 (2.34-19.04)	<0.001	7.84 (2.85-21.56)	<0.001
Systolic, per 24 mm Hg increase	1.28 (1.09-1.49)	0.002	1.17 (1.02-1.34)	0.023
HDL, per 16 md/dL increase	0.81 (0.71-0.94)	0.004	-	-
Ethnicity				
Non-Asian	1.00 (ref.)	-		
Asian	1.60 (1.14-2.26)	0.007	-	-
Stroke or TIA	1.65 (1.10-2.46)	0.015	1.54 (1.14-2.34)	0.007
BMI	0.96 (0.93-0.99)	0.021		
Male sex	-	-	1.32 (1.05-1.68)	0.022
Regular alcohol consumption	1.45 (1.02-2.07)	0.038	1.38 (1.01-1.89)	0.041

A1/A2 means extra- or intracranial atherosclerotic stenosis ipsilateral to the cerebral ischemia or aortic arch atheroma ≥4 mm or aortic arch thrombus, A3 means atherosclerotic disease in any vascular bed (extra- or intracranial ipsilateral atherosclerosis <u>without</u> luminal stenosis or atherosclerotic stenosis or plaque in any artery but not ipsilateral to the cerebral ischemia or aortic arch atheroma <4 mm).

eTable 30. Multivariable Association Between Baseline Characteristics and ASCOD Grades S1-S2 and S1-S2 and S3 vs A0, S0, C0, O0, or D0

	S1/S2 OR (95%CI)	P-value	S1/S2/S3 OR (95%CI)	P-value
Acute infarction				
No	1.00 (ref.)	-	1.00 (ref.)	-
Single	3.24 (2.33-4.49)	<0.001	3.39 (2.45-4.69)	<0.001
Multiple	1.77 (1.09-2.89)	0.022	1.83 (1.13-2.99)	0.015
Regular physical activity	0.38 (0.27-0.54)	<0.001	0.36 (0.26-0.52)	<0.001
Age, per 10 years increase	1.38 (1.23-1.55)	<0.001	1.38 (1.23-1.55)	<0.001
Ethnicity				
Non-Asian	1.00 (ref.)	-	1.00 (ref.)	
Asian	2.31 (1.66-3.21)	<0.001	2.28 (1.64-3.17)	<0.001
Dyslipidemia	1.77 (1.31-2.38)	<0.001	1.76 (1.30-2.36)	<0.001
Hypertension	1.63 (1.21-2.19)	0.001	1.65 (1.23-2.21)	0.001
Systolic, per 24 mm Hg increase	1.29 (1.10-1.52)	0.002	1.29 (1.10-1.51)	0.001
Living alone	1.52 (1.13-2.05)	0.006	1.43 (1.07-1.93)	0.018
ABCD2 score				
0-3	1.00 (ref.)	-	1.00 (ref.)	
4-5	1.45 (1.03-2.04)	0.034	1.49 (1.06-2.10)	0.024
6-7	1.77 (1.13-2.76)	0.012	1.81 (1.16-2.83)	0.009
Male sex	1.38 (1.04-1.82)	0.025	-	-
Regular alcohol consumption	-	-	1.44 (1.00-2.07)	0.050

S1/S2 means new small deep infarct of lacunar type, single (S2) or associated with old small deep infarct(s), and/or Fazekas-3 leukoaraiosis, and/or microdeposit of hemosiderin (S1); S3 means Fazekas-3 leukoaraiosis, and/or multiple old lacunes, and/or microdeposit of hemosiderin.

eTable 31. Multivariable Association Between Baseline Characteristics and ASCOD Grades C1-C2 and C1-C2 and C3 vs A0, S0, C0, O0, or D0

	OR (95%CI)	P-value	OR (95%CI)	P-value
Age, per 10 years increase	1.51 (1.35-1.68)	<0.001	1.34 (1.21-1.47)	<0.001
Atrial fibrillation or flutter	38.6 (14.0-106.1)	<0.001	27.03 (9.88-73.97)	<0.001
Acute infarction				
No	1.00 (ref.)	-	1.00 (ref.)	-
Single	2.46 (1.73-3.50)	<0.001	2.40 (1.76-3.29)	<0.001
Multiple	3.91 (2.45-6.24)	<0.001	3.13 (2.02-4.83)	<0.001
Hypertension	1.81 (1.32-2.48)	<0.001	1.47 (1.11-1.94)	0.006
Clinically significant valvular disease or prosthetic heart valve	9.32 (2.69-32.28)	<0.001	5.95 (1.77-20.03)	0.004
Regular physical activity	0.56 (0.40-0.79)	0.001	0.71 (0.53-0.95)	0.019
LDL, per 40 mg/dL increase	0.79 (0.66-0.94)	0.010	0.81 (0.70-0.94)	0.007
Regular alcohol consumption	1.60 (1.09-2.36)	0.017	1.50 (1.07-2.11)	0.020
Male sex	1.42 (1.06-1.91)	0.021	1.39 (1.07-1.80)	0.013

C_1/C_2 means cardiac pathology likely causal (C1), e.g., atrial fibrillation, significant valve disease, endocarditis, or possibly causal (C2), e.g., intracardiac spontaneous echo contrast, apical akinesia with left ejection fraction >35%, patent foramen ovale with atrial septal aneurysm; C3 means one of the following abnormalities present in isolation: patent formen ovale, atrial septal aneurysm, strands, mitral annulus calcification, calcification aortic valve, nonapical akinesia of the left ventricle, transient atrial fibrillation <60 s, atrial hyperexcitability.

eFigure 1. Study Flowchart

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                    ┌─────────────────────────────────────┐
                    │ 4789 patients enrolled in the registry │
                    └─────────────────────────────────────┘
                               │
                               │        ┌──────────────────────────────────────────┐
                               │        │ 173 did not meet inclusion criteria        │
                               ├────────│ 33 had no follow-up                        │
                               │        │ 736 patients excluded (17 centres with less than │
                               │        │ 50% of 5 years follow-up visit)            │
                               │        └──────────────────────────────────────────┘
                               │
                    ┌─────────────────────────┐
                    │ 3847 patients in TIA registry │
                    └─────────────────────────┘
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1406 A0	998 A1/A2	1108 A3	335 A9
2141 S0	773 S1/S2	912 S3	21 S9
2733 C0	800 C1/C2	226 C3	88 C9
3392 O0/D0	206 O1/D1 or O2/D2	249 O3/D3	

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                    ┌──────────────────────────────┐
                    │ 484 patients A0S0C0O0D0        │
                    └──────────────────────────────┘
```
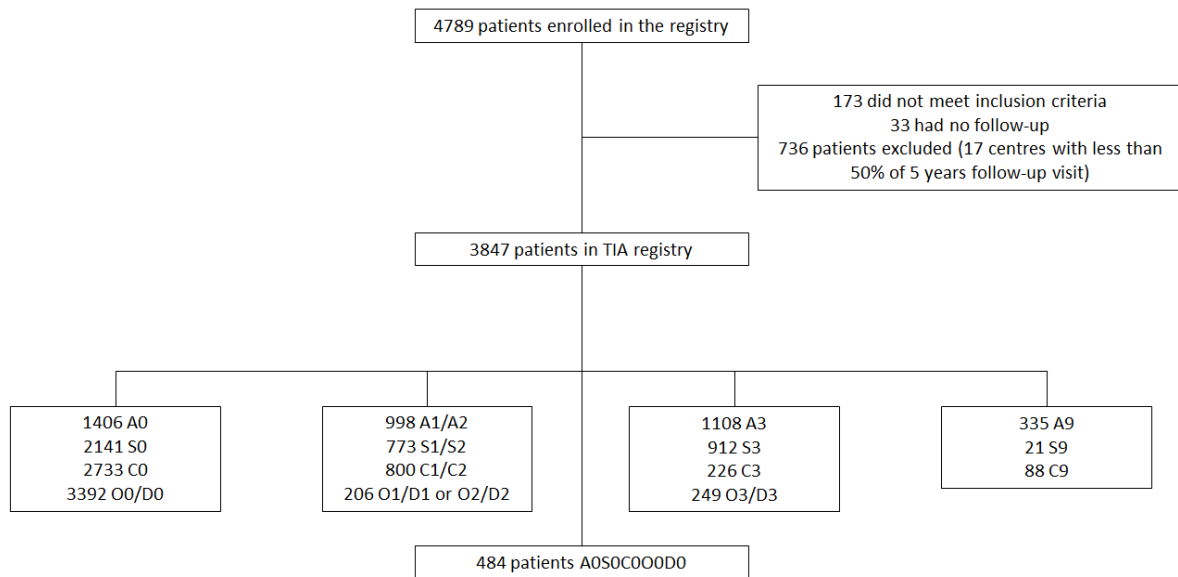
A: atherosclerosis, S: Small vessel disease, C: Cardiac pathology, O: Other causes, D: Dissection

0: disease is absent

1: disease is present, likely causal

2: disease is present, possibly causal

3: disease is present, unlikely causal

9: disease has not been assessed properly

eFigure 2. Venn Diagram Among Main ASCOD Diseases (Atherosclerosis, Small Vessel Disease, and Cardiac Pathology)

1: disease is present and potentially directly causal; 2: disease is present and possibly directly causal; 3: disease is present and not directly related with the stroke, e.g., contralateral to the ischemic field)
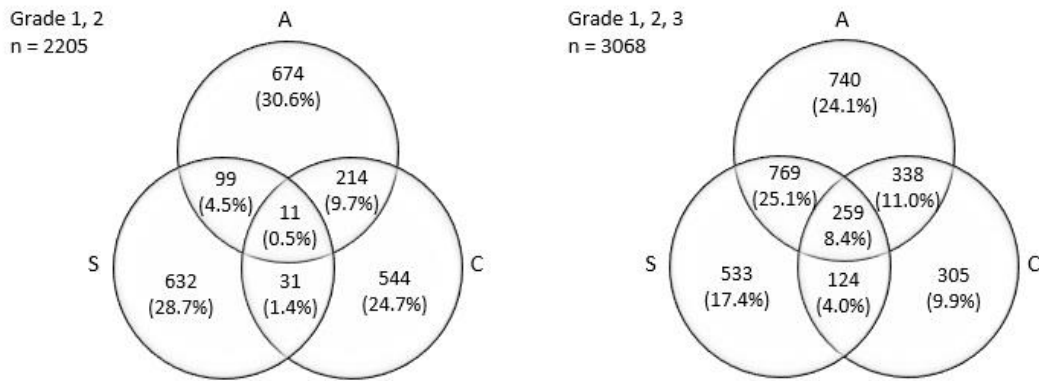
eFigure 3. Five-Year Cumulative Incidence of Recurrent Major Cardiovascular Event According to ASCOD Grades S0, S1-S2, and S3
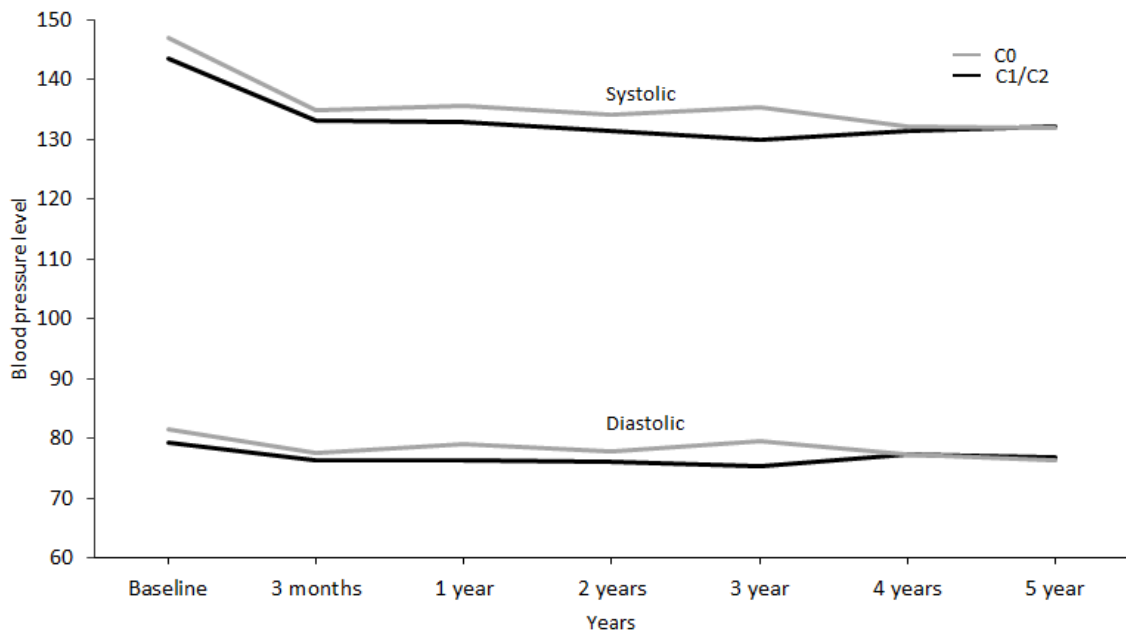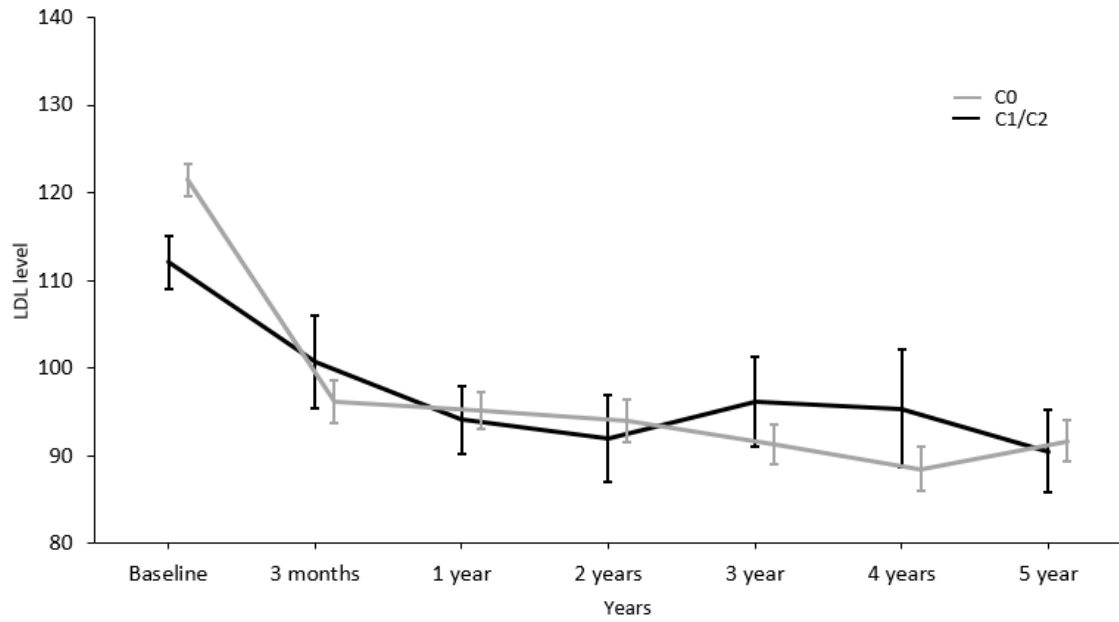

	0	1	2	3	4	5
S0	2141	1946	1809	1706	1621	1255
S1/S2	773	705	655	616	576	458
S3	912	801	733	666	619	474
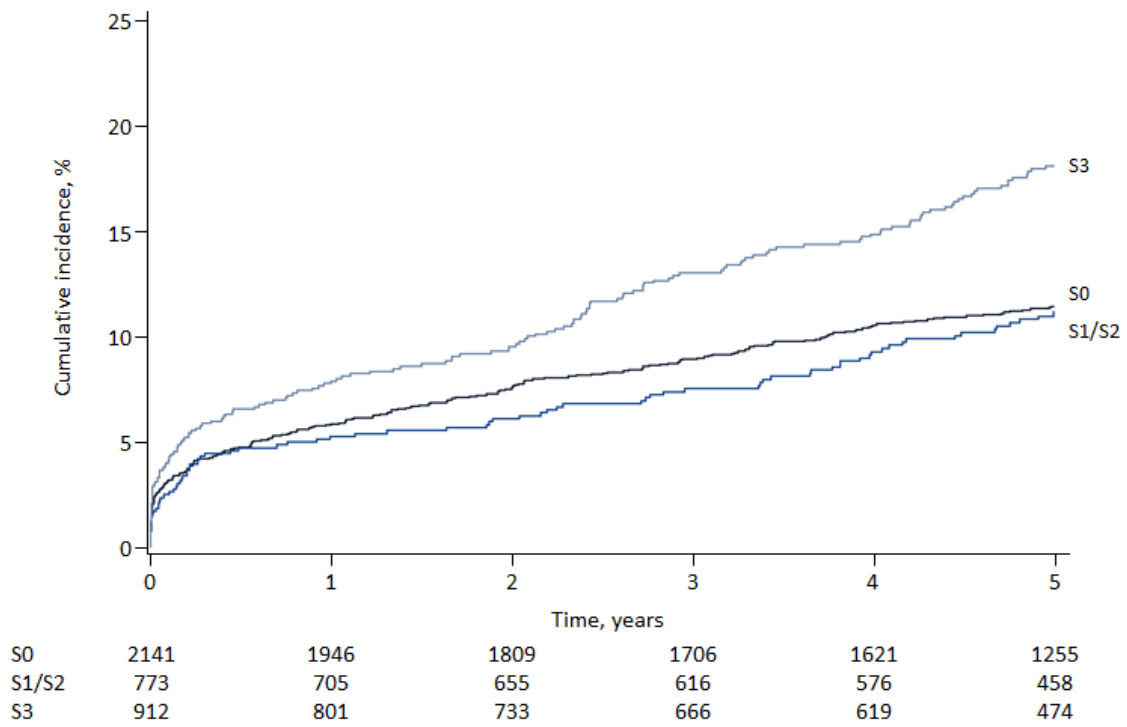
eFigure 4. LDL and Blood Pressure Evolution: Small Vessel Disease
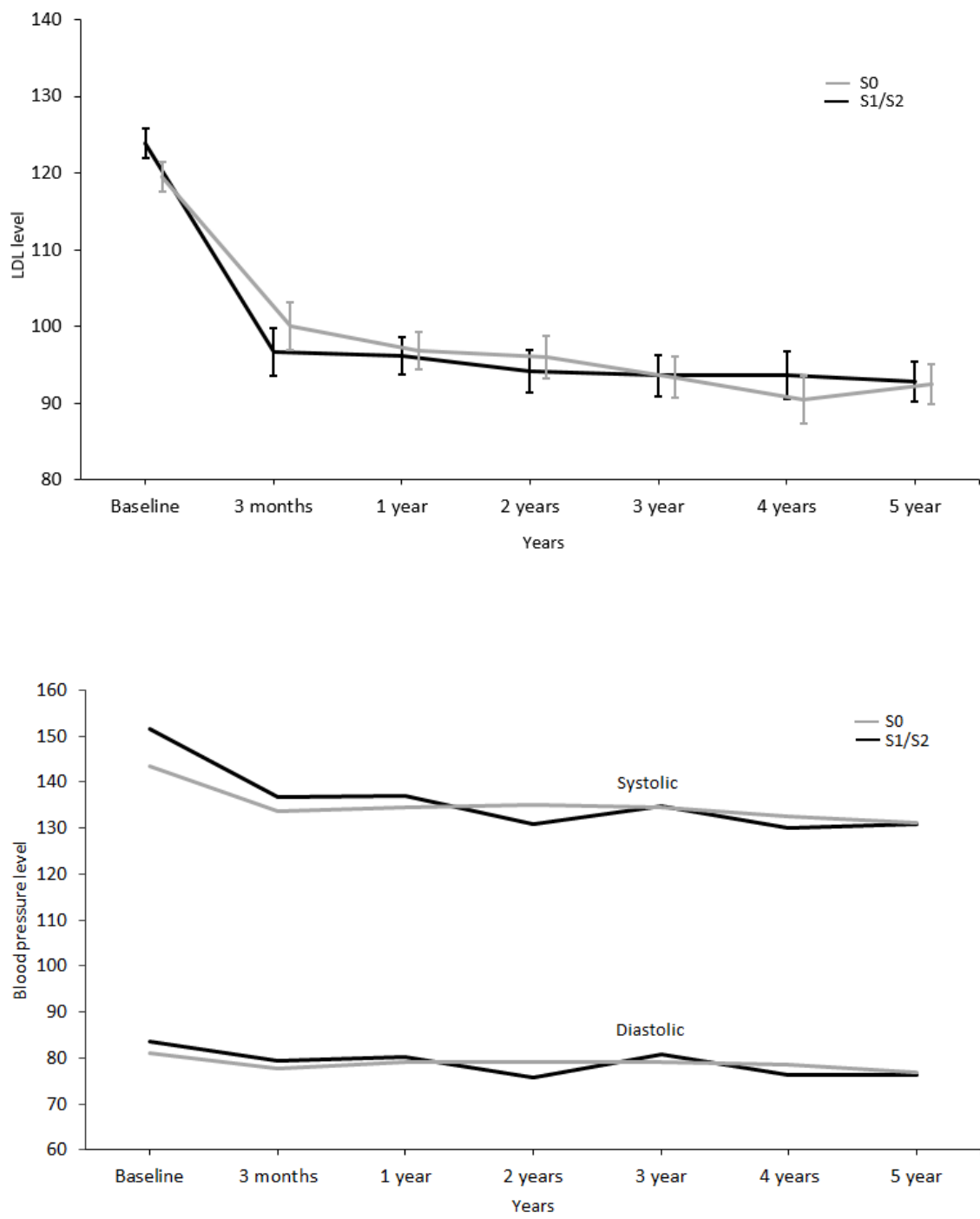
eFigure 5. Five-Year Cumulative Incidence of Recurrent Major Cardiovascular Event According to ASCOD Grades C0, C1-C2, and C3

C0	2733	2479	2304	2156	2043	1590
C1/C2	800	700	636	584	538	402
C3	226	211	198	191	184	151
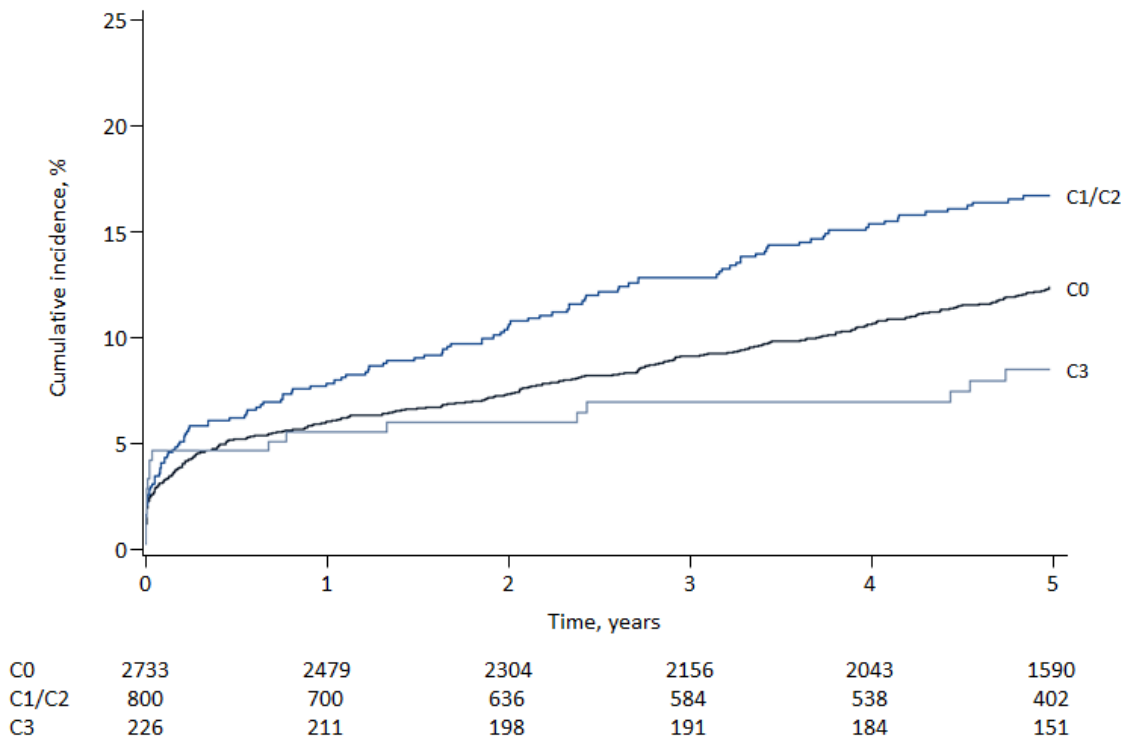
eFigure 6. LDL and Blood Pressure Evolution: Cardiac Pathology

eFigure 7. Five-Year Cumulative Incidence of Recurrent Major Cardiovascular Event According to ASCOD Grades O0-D0, O1-D1, or O2-D2 and O3-D3
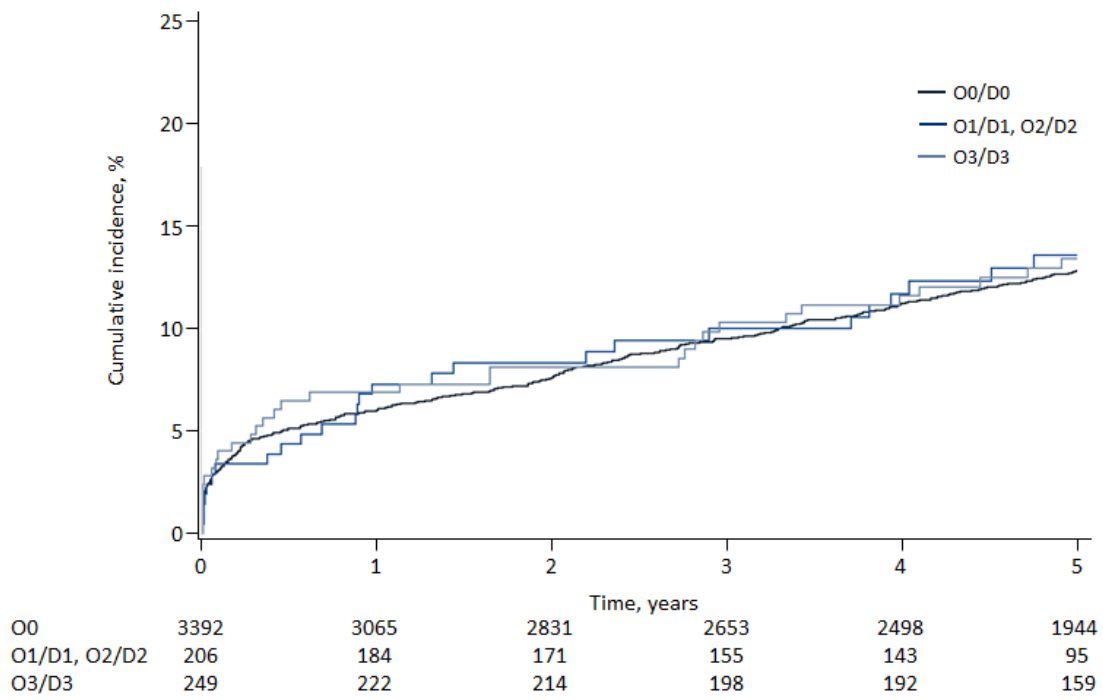
eFigure 8. LDL and Blood Pressure Evolution: Other Causes and Dissection
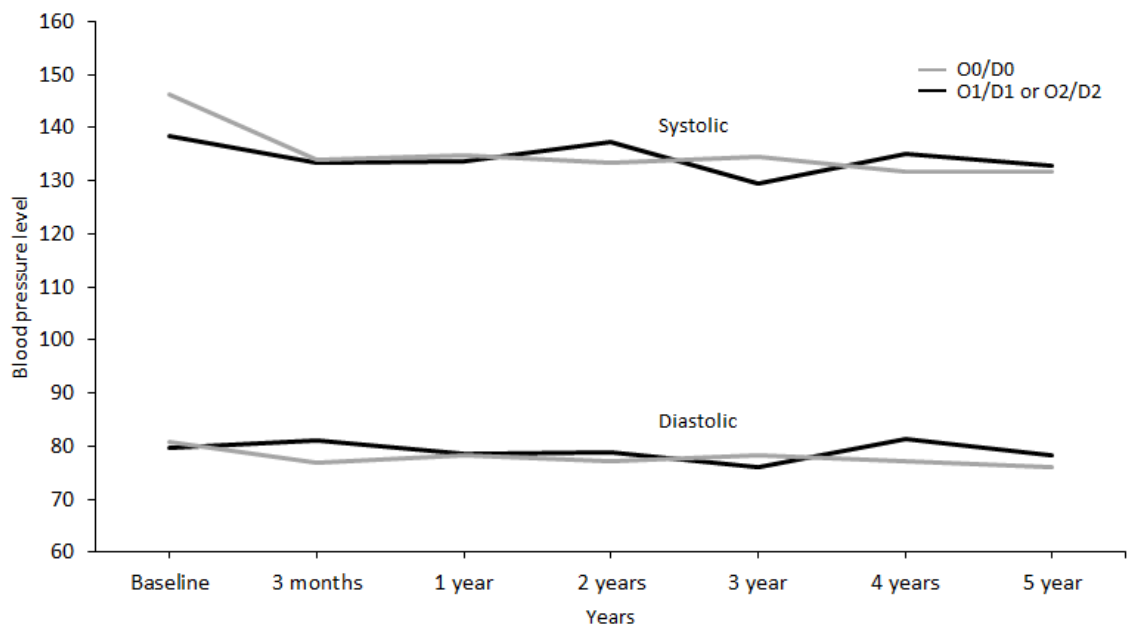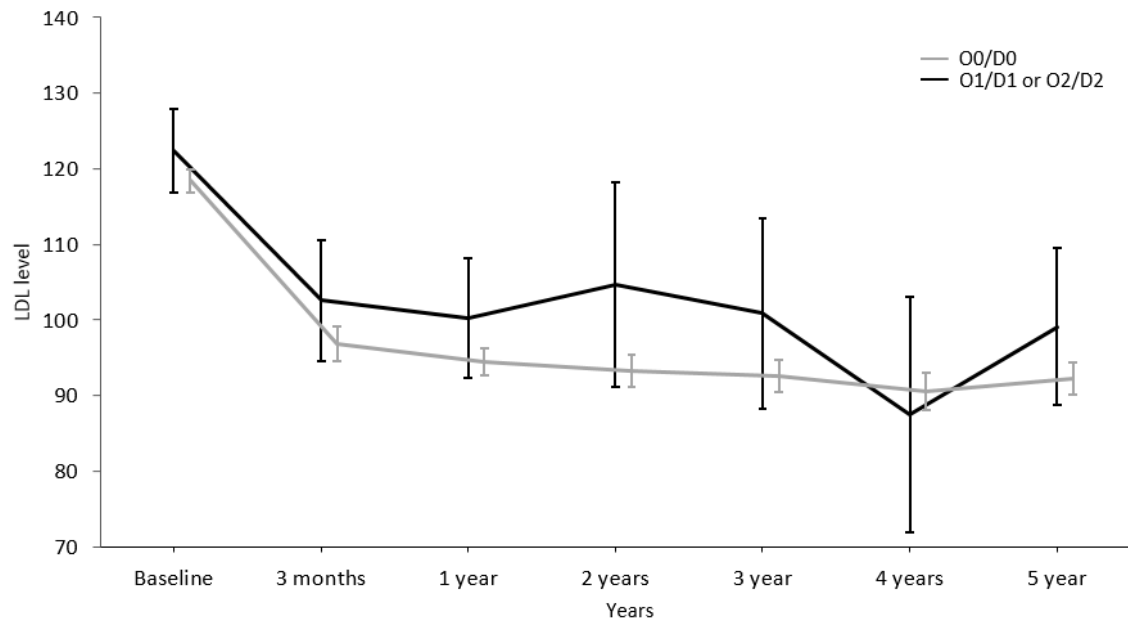
eFigure 9. Five-Year Cumulative Incidence of Recurrent Major Cardiovascular Event According to ASCOD Grades A1-A2 and A3, S1-S2 and S3, C1-C2 and C3, O1-O2 and O3, D1-D2 and D3, and A0, S0, C0, O0, or D0
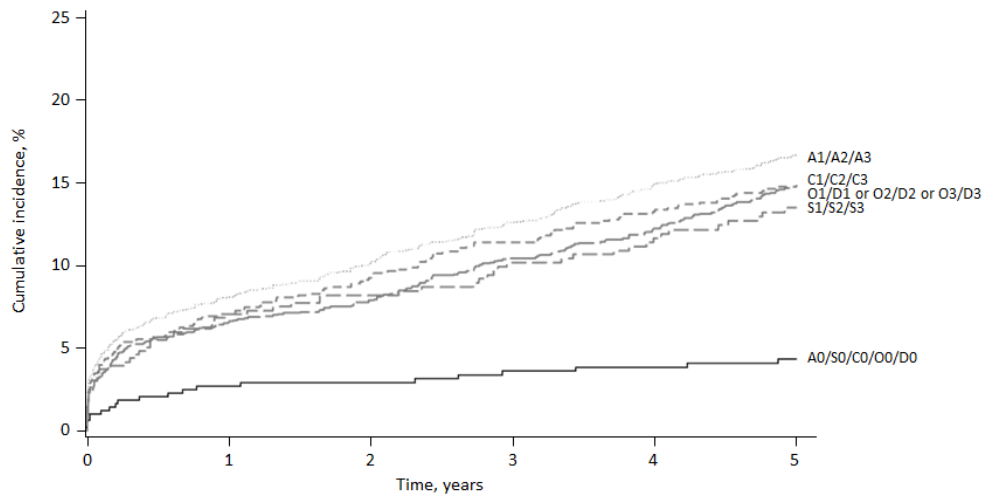
eMethods 1. ASCOD Phenotyping: Method of Classification[4]

Method of classification[4]

Grades of diseases	
1	If the disease is present and can potentially be a cause
2	If the disease is present, but the causal link is uncertain
3	If the disease is present, but the causal link is unlikely
0	If the disease is absent
9	If the work up is insufficient to grade the disease

A : Causality grades for Atherothrombosis

A1 « Potentially causal »	*Atherothrombotic stroke* defined as: (1) Ipsilateral atherosclerotic stenosis between 50–99% in an intra-/or extracranial artery supplying the ischemic field; **or** (2) Ipsilateral atherosclerotic stenosis <50% in an intra-/or extracranial artery with an endoluminal thrombus supplying the ischemic field; **or** (3) Mobile thrombus in the aortic arch; **or** (4) Ipsilateral arterial occlusion in an intra-/or extracranial artery with evidence of underlying atherosclerotic plaque supplying the ischemic field
A2 "Causal link is uncertain"	(1) Ipsilateral atherosclerotic stenosis 30-50% in an intra-/or extracranial artery supplying the ischemic field; **or** (2) Aortic plaque ≥4 mm without mobile lesion.
A3 "Causal link is unlikely, but the disease is present"	(1) Plaque (stenosis <30%) in an intra- or extracranial artery, ipsilateral to the infarct area (2) Aortic plaque <4 mm without mobile thrombus; (3) Stenosis (any degree) or occlusion in a cerebral artery not supplying the infarct area (e.g., contralateral side or opposite circulation) (4) History of myocardial infarction, coronary revascularization or peripheral arterial disease. (5) Ipsi- or bilateral atherosclerotic stenosis 50-99% with bi-hemispheric MR-DWI-lesion
A0 "Atheroscleosis not detected"	**Ruling out atheroscleosis**: (1) Extracranial arterial stenosis: one or several of the following diagnostic tests are performed and negative US-Duplex, CTA, MRA, XRA, or autopsy. (2) Intracranial arterial stenosis: one or several of the following diagnostic tests are performed and are negative: US-TCD, MRA, CTA, XRA, or autopsy. (3) Aortic arch atheroma: TEE with <u>specific assessment</u> of the aortic arch (when the probe is pulled back at the end of the cardiac examination, turn the probe counter clockwise and take time to watch the aortic arch) or specific aortic arch assessment with CTA.
A9 "Incomplete work-up"	US-Duplex, US-TCD or CTA, or MRA, or XRA or autopsy not performed. [A minimum work-up is extra and intracranial assessment of cerebral arteries – maximum also include transesophageal assessment of the aortic arch (or a default CT angiography of the aortic arch)].

S : Causality grades for Small Vessel Disease

S1 « Potentially causal »	Combination of: *(1) Lacunar infarction:* small deep infarct <15 mm (in perforator branch territory) on MRI-DWI (or a default CT) in an area corresponding to the symptoms **and at least one of the three following criteria:** (2) one or several small deep **older** infarct(s) of lacunar type in other territories ; **and/or** (3) severe (confluent –Fazekas III) leukoaraiosis, or microbleeds, or severe dilatation of perivascular spaces (« état criblé »). (4) repeated, recent -<1 month-, TIAs attributable to the same territory as the index infarct
S2 "Causal link is uncertain"	(1) <u>Only one</u>, recent, lacunar infarction and no other abnormality on MRI (or CT) **or** (2) Clinical syndrome suggestive of a deep branch artery stroke, without ischemic lesion in the appropriate area seen on MRI or CT [Main clinical syndrome suggesting a deep branch artery –lacunar– stroke : pure hemiparesis, pure hemi sensory loss, Hemiparesis-ataxy, Dysarthria clumsy hand syndrome, unilateral sensory-motor deficit, others: hemichorea, hemiballism, pure dysarthria, etc.)]
S3 "Causal link is unlikely, but the disease is present"	Severe (confluent-Fazekas III) leukoaraiosis visible on MRI and/or CT scan, and/or microbleeds visible on T2*-weighted MRI, and/or severe dilatation of perivascular spaces (visible on T2-weighted MRI), and/or one or several old, small deep infarcts of lacunar type
S0 "Small vessel disease not detected"	**Ruling out small vessel disease stroke:** negative MRI (T2, FLAIR, GRE, DWI) and no appropriate clinical syndrome suggestive of a deep branch artery stroke
S9 "Incomplete work-up"	MRI (or CT) not performed

C : Causality grades for Cardiac pathology

C1 « Potentially causal »	Cardiogenic stroke defined as acute, or recent and older bi-hemispheric or supra- and infra-tentorial territorial or cortical ischemic lesions and signs of systemic embolism <u>with detection of at least one of the following potential causes</u>: (1) Mitral stenosis (surface <1.5 cm^2); (2) Mechanical valve; (3) Myocardial infarction within 4 weeks preceding the cerebral infarction; (4) Mural thrombus in the left cavities; (5) Aneurysm of the left ventricle; (6) history or presence of documented atrial fibrillation –whether paroxysmal (>60 sec),, persistent or permanent- or flutter, with or without left atrial thrombus or spontaneous echo; (7) Atrial disease (tachycardia-bradycardia syndrome); (8) Dilated or hypertrophic cardiomyopathies; (9) Left ventricle ejection fraction <35%; (10) Endocarditis; (11) Intracardiac mass; (12) PFO **and** thrombus in situ; (13) PFO **and *concomitant*** pulmonary embolism or proximal DVT ***<u>preceding</u>*** <u>*the index cerebral infarction*</u> (14) Aforementioned cardiac pathologies (C1) with single or without obvious cerebral ischemic lesion
C2 "Causal link is uncertain"	Regardless of stroke pattern: (1) PFO + atrial septal aneurysm, (2) PFO <u>and</u> pulmonary embolism or proximal DTV <u>*concomitant but NOT preceding*</u> the index cerebral infarction, (3) intracradiac spontaneous echo-contrast, (4) Apical akinesia of the left ventricle <u>and</u> decreased ejection fraction (but >35%) ; (5) History of Myocardial infarction or palpitation <u>and</u> multiple brain infarction, repeated either bilateral or in two different arterial territories (e.g., both anterior and posterior circulation) ; (6) no direct cardiac source identified, but multiple brain infarction, repeated either bilateral or in two different arterial territories (e.g., both anterior and posterior circulation) and/or evidence of systemic emboli : renal or splenic or mesenteric infarction (on CT, MRI or autopsy) or embolism in peripheral artery supplying arm or leg.
C3 "Causal link is unlikely, but the disease is present"	One of the following abnormalities present in isolation: PFO, ASA, strands, mitral annulus calcification, calcification aortic valve, non apical akinesia of the left ventricle, transient atrial fibrillation <60sec, atrial hyperexcitability
C0 "Cardiac pathology not detected or not suspected"	**Ruling out a cardiac source of embolism**: minimum is negative ECG and examination by a cardiologist; maximum is negative ECG/telemetry/24-hour Holter ECG/long-term ECG recording (implantable device, transtelephonic ECG, loop recorder) and negative TEE for atrium, valves and septal abnormalities, negative TTE for PFO and assessment of left ventricle, negative cardiac CT/MRI, negative abdominal CT/MRI (search for old or simultaneous subdiaphragmatic visceral infarction)
C9 "Incomplete work-up**"**	Minimum is ECG and examination by a trained cardiologist in the absence of cardiac imaging

O : Causality grades for Other Causes

O1 "Potentially causal"	(1) Dolichoectasia with complicated aneurysm (2) Polycythemia vera or thrombocythemia >800 000/mm³ (3) Systemic Lupus (4) disseminated intravascular coagulation (5) Antiphospholipid antibody syndrome (including >100 GPL units or lupus anticoagulant) (6) Fabry's disease (7) Co-existing meningitis (8) sickle cell disease (9) Ruptured intracranial aneurysm with or without vasospasm of the artery supplying the infarcted area (10) severe hyperhomocysteinemia; (11) Horton's disease; (12) other cerebral inflammatory or infectious angeitis; (13) Moya-Moya etc….
O2 "Causal link is uncertain"	(1) Saccular aneurysm (with a suspicion of embolism from it) (2) coincidental migraine attack with neurological deficit lasting >60 min in patients with history of migraine aura
O3 "Causal link is unlikely" but the disease is present"	(1) Arterio-venous malformation; (2) thrombocythosis <800 000/mm³, (3) antiphospholipid antibody <100 GPL units (4) homocysteinemia <40 μmol/L (5) malignoma with associated hypercoagulation (high d-dimer levels), deep vein thrombosis or pumlmonary embolism and/or recent chemotherapy
O0 "No other cause detected"	**Ruling out other causes**: negative: cerebrospinal fluid, complete haemostasis, cerebral arterial imaging, family history of inherited disease, inflammatory markers (erythrocyte sedimentation rate, C-reactive protein), hematologic tests (platelet, leucocytes, and eosinophilic counts, hematocrit), specific tests according to the suspected disease (e.g., genetic test, retinal angiography for Susac syndrome)
O9 "Incomplete work-up"	Unable to reasonably exclude other causes based on best available diagnostic tests and stroke specific history

D : Causality grades for Dissection

D1 "Potentially causal"	(1) Arterial dissection by direct demonstration (evidence of mural hematoma: hypersignal on Fat-saturated MRI or at autopsy or on TOF-MRA or CT on axial sections showing both enlargement of the arterial wall by the hematoma with narrowing of the lumen- or on echography showing an hypoechoic arterial wall with narrowing of the lumen and sudden enlargement of the carotid or vertebral (V2) artery diameter. (2) Arterial dissection by indirect demonstration or by less sensitive or less specific diagnostic test (only long arterial stenosis beyond the carotid bifurcation or in V2, V3 or V4 without demonstration of arterial wall hematoma : on X-ray angiography, and/or echography and/or CTA and/or MRA) or unequivocal US with recanalization during follow-up
D2 "Causal link is uncertain"	(1) arterial dissection by weak evidence (suggestive clinical history, e.g., painful Horner's syndrome or past-history of arterial dissection) (2) Imaging evidence of fibromuscular dysplasia of a cerebral artery supplying the ischemic field
D3 "Causal link is unlikely" but the disease is present"	(1) Kinking or dolichoectasia without complicated aneurysm or plicature, (2) Fibromuscular dysplasia on arteries not supplying the ischemic field;
D0 "No dissection detected or suspected"	**Ruling out dissection** : negative FAT saturated MRI of suspected artery or good-quality, normal X-ray angiography [too early FAT saturated MRI performed within 3 days of symptom onset can be falsely negative and then should be repeated]. If there is no clinical suspicion of dissection the patient can be classified D0 provided good quality extra-/intra-cranial cerebral arteries and cardiac evaluations have been performed.
D9 "Incomplete work-up"	In patients aged less than 60 years and no evidence of A1, A2, S1, C1, or O1 category : No FAT saturated MRI performed on the extra or intracranial artery supplying the ischemic field or no X-ray angiography performed (all performed within 15 days of symptom onset).