SUPPLEMENTAL MATERIAL

Supplementary Tables

Table S1. Baseline clinical and biochemical characteristics of both included and excluded patients.

	Included patients (n=1,441)	Excluded patients (n=1,772)	Total (n=3,213)	*p* value
Age, years (mean ± SD)	73.5 ± 9.7	73.7 ± 10.0	73.6 ± 9.9	0.541
Male, n (%)	750 (52.0)	900 (50.8)	1650 (51.4)	0.501
Body mass index	23.3 ± 3.3	23.3 ± 3.5	23.3 ± 3.4	0.677
History of risk factors, n (%)				
Hypertension	1026 (71.2)	1201 (67.8)	2227 (69.3)	0.040
Diabetes mellitus	410 (28.5)	446 (25.2)	856 (26.6)	0.040
Dyslipidemia	313 (21.7)	455 (25.7)	768 (23.9)	0.010
Congestive heart failure	56 (3.9)	85 (4.8)	141 (4.4)	0.243
Current smoking	204 (14.2)	226 (12.8)	430 (13.4)	0.267
Prior stroke or TIA	454 (31.5)	604 (34.1)	1058 (32.9)	0.131
Biochemical variables (mean ± SD)				
LDL-C, mg/dL	98.1 ± 34.1	93.7 ± 36.1	95.8 ± 35.2	0.001
Triglyceride, mg/dL	96.9 ± 58.3	98.4 ± 62.9	97.7 ± 60.7	0.511
HDL-C, mg/dL	47.8 ± 18.5	53.2 ± 26.7	50.6 ± 23.3	<0.001
Glycated hemoglobin, %	6.0 ± 1.7	6.1 ± 2.0	6.1 ± 1.9	0.190
Admission glucose, mg/dL	138.7 ± 71.2	142.2 ± 69.5	140.5 ± 70.3	0.176
Creatinine clearance, mL/min	62.3 ± 28.3	61.6 ± 29.9	61.9 ± 29.2	0.527
Pre-stroke mRS, median (IQR)	0 (0;1)	0 (0;1)	0 (0;1)	0.098
Initial NIHSS, median (IQR)	9 (2;15)	8 (2;15)	8 (2;15)	0.625
Intravenous alteplase, n (%)	327 (22.7)	393 (22.2)	720 (22.4)	0.760
Mechanical thrombectomy, n (%)	207 (14.4)	165 (9.3)	372 (11.6)	<0.001
CHA_2DS_2-VASc score, median (IQR)	5 (4; 6)	5 (4; 6)	5 (4; 6)	0.238

SD, standard deviation; TIA, transient ischemic attack; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; mRS, modified Rankin Scale; IQR, interquartile ranges; NIHSS, National Institutes of Health Stroke Scale.

Table S2. Baseline characteristics according to antithrombotic therapy.

	Antiplatelets (n=323)	Anticoagulants (n=1,118)	Total (n=1,441)	*p* value
Age, years (mean ± SD)	73.8 ± 9.0	73.4 ± 9.8	73.5 ± 9.7	0.509
Male, n (%)	167 (51.7)	583 (52.1)	750 (52.0)	0.938
AF type, n (%)				<0.001
Paroxysmal AF	248 (76.8)	590 (52.8)	838 (58.2)	
Sustained AF	75 (23.2)	528 (47.2)	603 (41.8)	
Body mass index	23.3 ± 3.3	23.3 ± 3.3	23.3 ± 3.3	0.951
History of risk factors, n (%)				
Hypertension	225 (69.7)	801 (71.6)	1026 (71.2)	0.532
Diabetes mellitus	93 (28.8)	317 (28.4)	410 (28.5)	0.933
Dyslipidemia	46 (14.2)	267 (23.9)	313 (21.7)	<0.001
Congestive heart failure	5 (1.5)	51 (4.6)	56 (3.9)	0.021
Current smoking	46 (14.2)	158 (14.1)	204 (14.2)	1.000
Prior stroke or TIA	104 (32.2)	350 (31.3)	454 (31.5)	0.813
Biochemical variables (mean ± SD)				
D-dimer, μg/mL	3.0 ± 5.0	2.6 ± 4.5	2.7 ± 4.6	0.235
LDL-C, mg/dL	96.9 ± 34.5	98.5 ± 34.0	98.1 ± 34.1	0.473
Triglyceride, mg/dL	92.1 ± 48.8	98.3 ± 60.7	96.9 ± 58.3	0.056
HDL-C, mg/dL	47.5 ± 17.1	47.9 ± 18.9	47.8 ± 18.5	0.699
Glycated hemoglobin, %	5.9 ± 1.2	6.0 ± 1.9	6.0 ± 1.7	0.219
Admission glucose, mg/dL	139.0 ± 50.3	138.6 ± 76.2	138.7 ± 71.2	0.924
Creatinine clearance, mL/min	62.2 ± 27.5	62.3 ± 28.5	62.3 ± 28.3	0.960
Pre-stroke mRS, median (IQR)	0 (0;3)	0 (0;1)	0 (0;1)	<0.001
Initial NIHSS, median (IQR)	10 (3;16)	9 (2;15)	9 (2;15)	0.031

Intravenous alteplase, n (%)	77 (23.8)	250 (22.4)	327 (22.7)	0.629
Mechanical thrombectomy, n (%)	45 (13.9)	162 (14.5)	207 (14.4)	0.871
CHA_2DS_2-VASc score, median (IQR)	5 (4; 6)	5 (4; 6)	5 (4; 6)	0.186
AIS presumed arterial origin, n (%)	101 (31.3)	337 (30.1)	438 (30.4)	0.750
Symptomatic atherosclerosis, n (%)	239 (74.0)	774 (69.2)	1013 (70.3)	0.114
Large artery atherosclerosis, n (%)				
Carotid atherosclerosis	109 (36.2)	305 (30.8)	414 (32.1)	0.093
Intracranial atherosclerosis	213 (69.4)	749 (74.6)	962 (73.4)	0.082
Coronary atherosclerosis	42 (13.0)	171 (15.3)	213 (14.8)	0.351
Peripheral atherosclerosis	1 (0.3)	20 (1.8)	21 (1.5)	0.091
OACs with antiplatelets, n (%)	-	295 (26.4)	295 (26.4)	-

AF, atrial fibrillation; TIA, transient ischemic attack; SD, standard deviation; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; IQR, interquartile ranges; AIS, acute ischemic stroke; LA, left atrium; LVEF, left ventricular ejection fraction; LV, left ventricle.

Table S3. Event rates and association estimates from Cox proportional hazard modeling according to antithrombotic therapy in all patients and patients with D-dimer levels of ≥2.0 μg/mL.

Clinical outcomes	All patients			Patients with D-dimer levels of ≥2.0 μg/mL		
	Antiplatelets (n=323)	OACs (n=1,118)	HR (95% CI); *p* value*	Antiplatelets (n=128)	OACs (n=387)	HR (95% CI); *p* value*
Primary outcome						
Recurrent ischemic stroke			0.81 (0.48-1.36); 0.421			0.44 (0.21-0.94); 0.028
Number of events	18	69		10	23	
Incidence per 100 person-years	5.07	3.95		11.10	4.74	
Secondary outcomes						
Any stroke			0.86 (0.53-1.40); 0.541			0.44 (0.22-0.93); 0.026
Number of events	20	81		11	26	
Incidence per 100 person-years	5.64	4.65		12.27	5.37	
Intracranial hemorrhage			0.99 (0.33-2.92); 0.979			0.31 (0.05-1.88); 0.203
Number of events	4	18		2	3	
Incidence per 100 person-years	1.08	1.00		2.15	0.59	
Acute coronary syndrome			0.84 (0.28-2.52); 0.756			0.94 (0.11-8.13); 0.953
Number of events	4	16		1	5	
Incidence per 100 person-years	1.09	0.89		1.07	1.00	
Major bleeding			1.05 (0.44-2.54); 0.910			1.03 (0.30-3.62); 0.959
Number of events	6	28		3	14	
Incidence per 100 person-years	1.62	1.56		3.20	2.79	

* Unadjusted hazard ratios and *p* values for anticoagulant therapy compared to antiplatelet therapy. OACs, oral anticoagulants; HR, hazard ratio; CI, confidence interval.

Table S4. Effects of high D-dimer levels (≥2.0 μg/mL) on primary and secondary outcomes in patients with paroxysmal and sustained atrial fibrillation (AF).

Outcomes	Patients with paroxysmal AF		Patients with sustained AF	
	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value
Primary outcome				
Recurrent ischemic stroke	2.39 (1.26−4.52)	0.007	1.35 (0.69−2.63)	0.373
Secondary outcomes				
Any stroke	2.26 (1.22−4.20)	0.009	1.17 (0.64−2.13)	0.610
Intracranial hemorrhage	1.62 (0.25−10.37)	0.607	0.43 (0.11−1.64)	0.223
Acute coronary syndrome	0.92 (0.24−3.45)	0.903	2.10 (0.30−14.74)	0.453
Major bleeding	2.14 (0.77−5.92)	0.143	1.73 (0.64−4.66)	0.276

HR, hazard ratio; CI, confidence interval.

Table S5. Adjusted hazard ratios for anticoagulant therapy compared with antiplatelet therapy in patients with the paroxysmal and sustained atrial fibrillation (AF) who presented high (≥2 μg/mL) baseline D-dimer levels.

Outcomes	Patients with paroxysmal AF		Patients with sustained AF	
	Adjusted HR (95% CI)	*p* value	Adjusted HR (95% CI)	*p* value
Primary outcome				
Recurrent ischemic stroke	0.52 (0.18−1.52)	0.237	0.17 (0.04−0.62)	0.007
Secondary outcomes				
Any stroke	0.45 (0.16−1.25)	0.128	0.24 (0.07−0.86)	0.028
Intracranial hemorrhage	NA	0.467	NA	0.967
Acute coronary syndrome	NA	0.982	0.14 (0.01−8.01)	0.187
Major bleeding	0.64 (0.13−3.18)	0.590	NA	0.986

HR, hazard ratio; CI, confidence interval; NA, not available.

Supplementary Figures

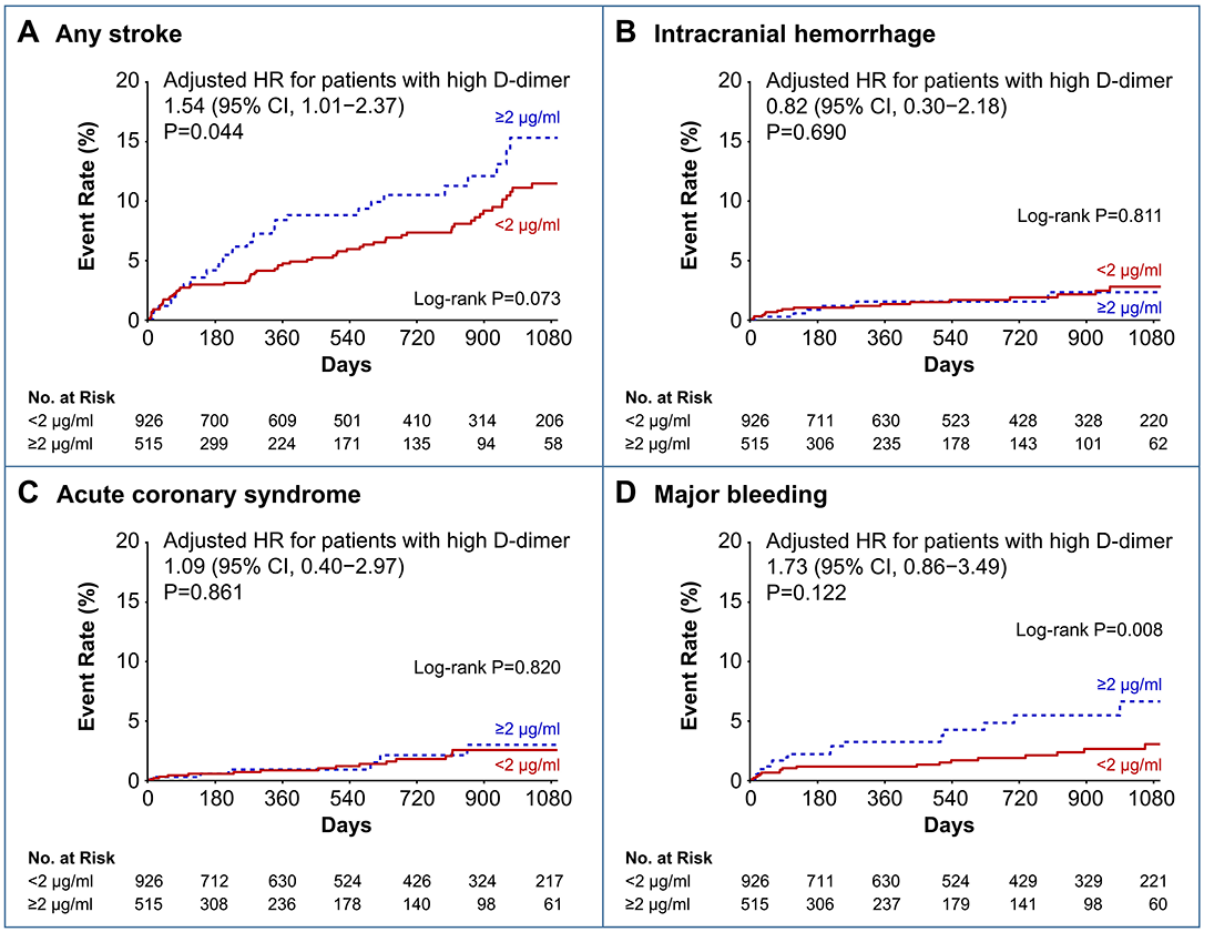

Figure S1. Kaplan-Meier curves and adjusted hazard ratios for secondary outcomes of (A) any stroke, (B) intracranial hemorrhage, (C) acute coronary syndrome, and (D) major bleeding according to the baseline D-dimer levels. HR, hazard ratio; CI, confidence interval.

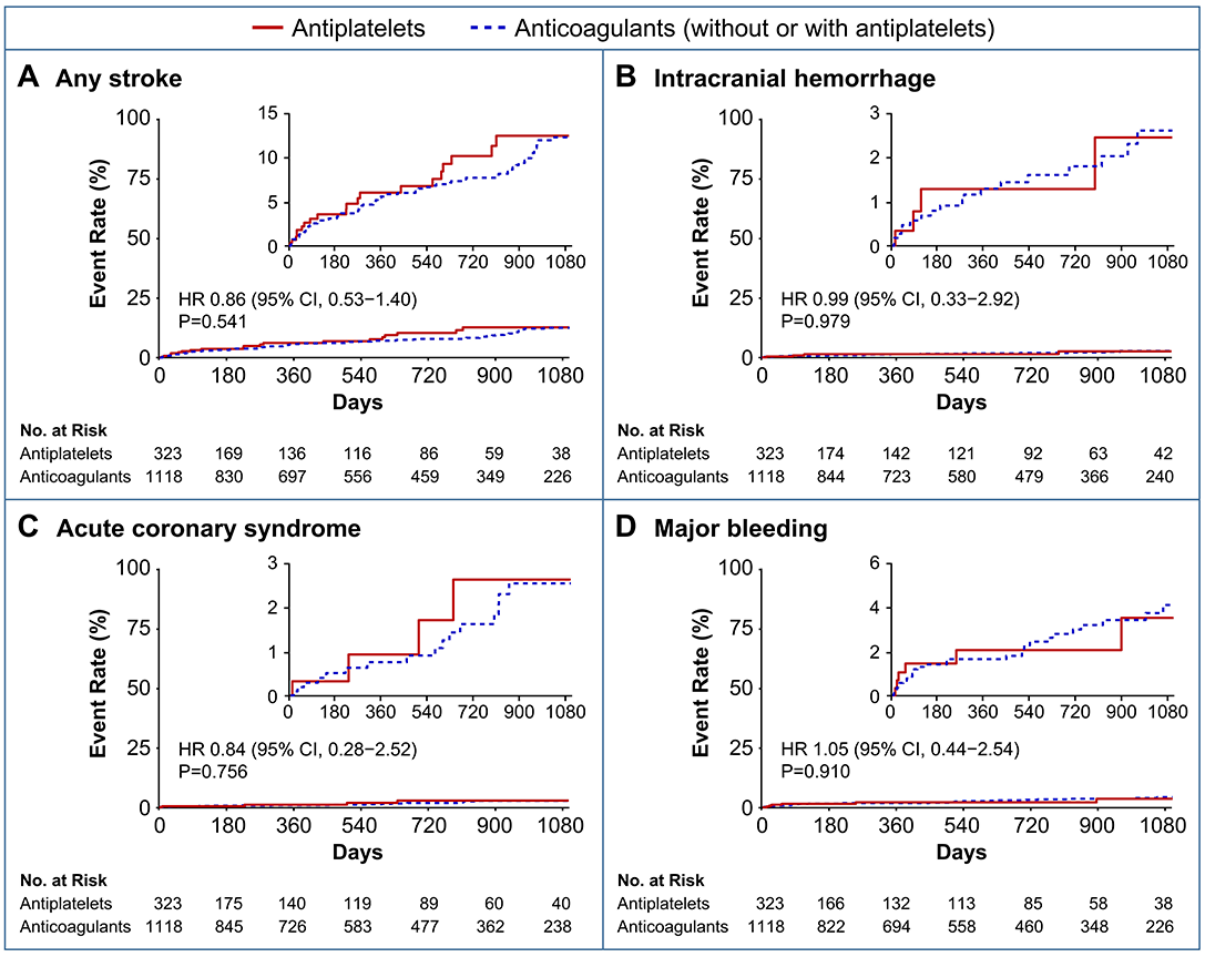

Figure S2. Kaplan-Meier curves for different types of stroke in all patients. Kaplan-Meier curves for (A) any stroke, (B) intracranial hemorrhage, (C) acute coronary syndrome, and (D) major bleeding according to antithrombotic therapy in all patients. HR, hazard ratio; CI, confidence interval.

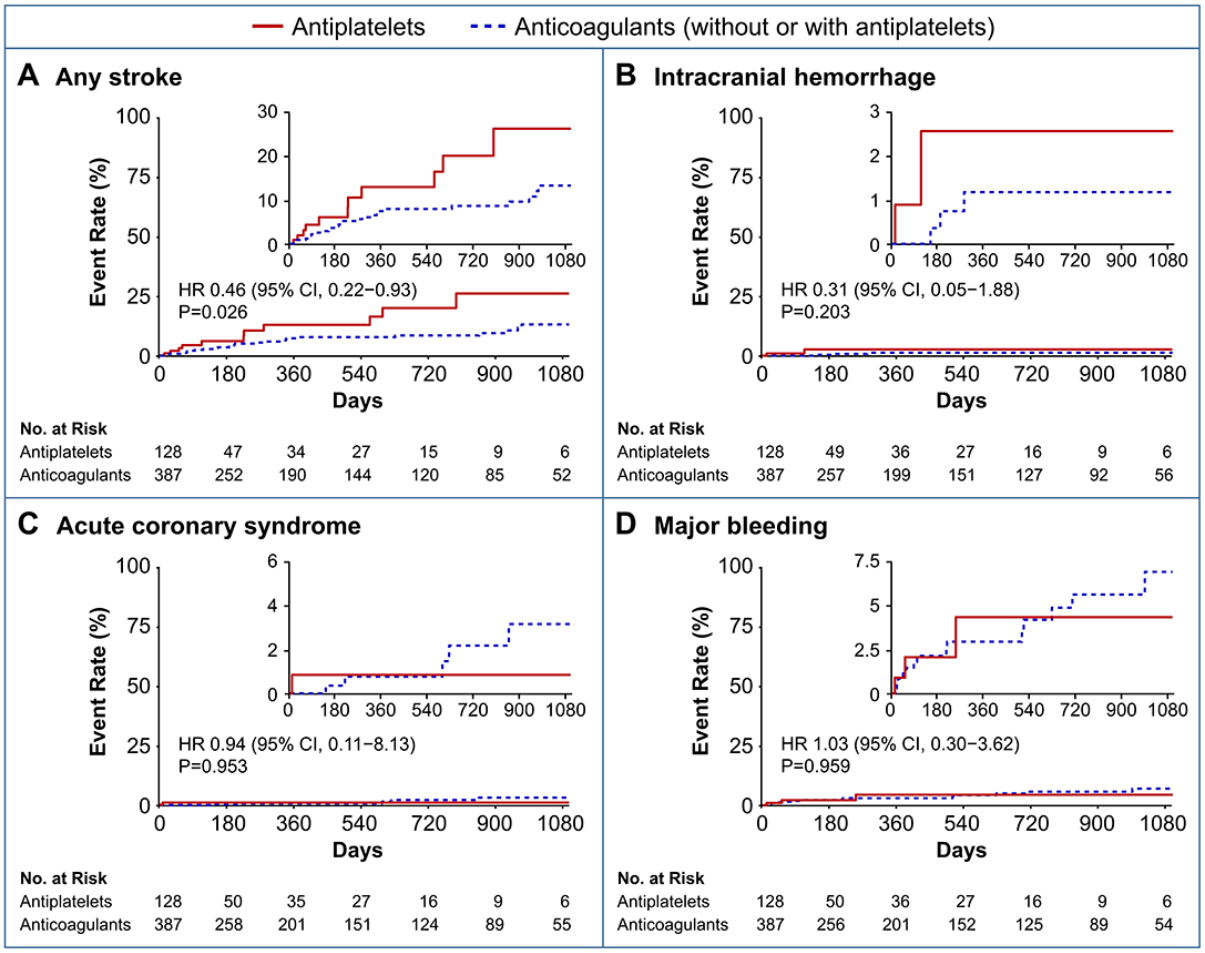

Figure S3. Kaplan-Meier curves for different types of stroke in patients with D-dimer levels of ≥2.0 μg/mL. Kaplan-Meier curves for (A) any stroke, (B) intracranial hemorrhage, (C) acute coronary syndrome, and (D) major bleeding according to antithrombotic therapy in patients with D-dimer levels of ≥2.0 μg/mL. HR, hazard ratio; CI, confidence interval.

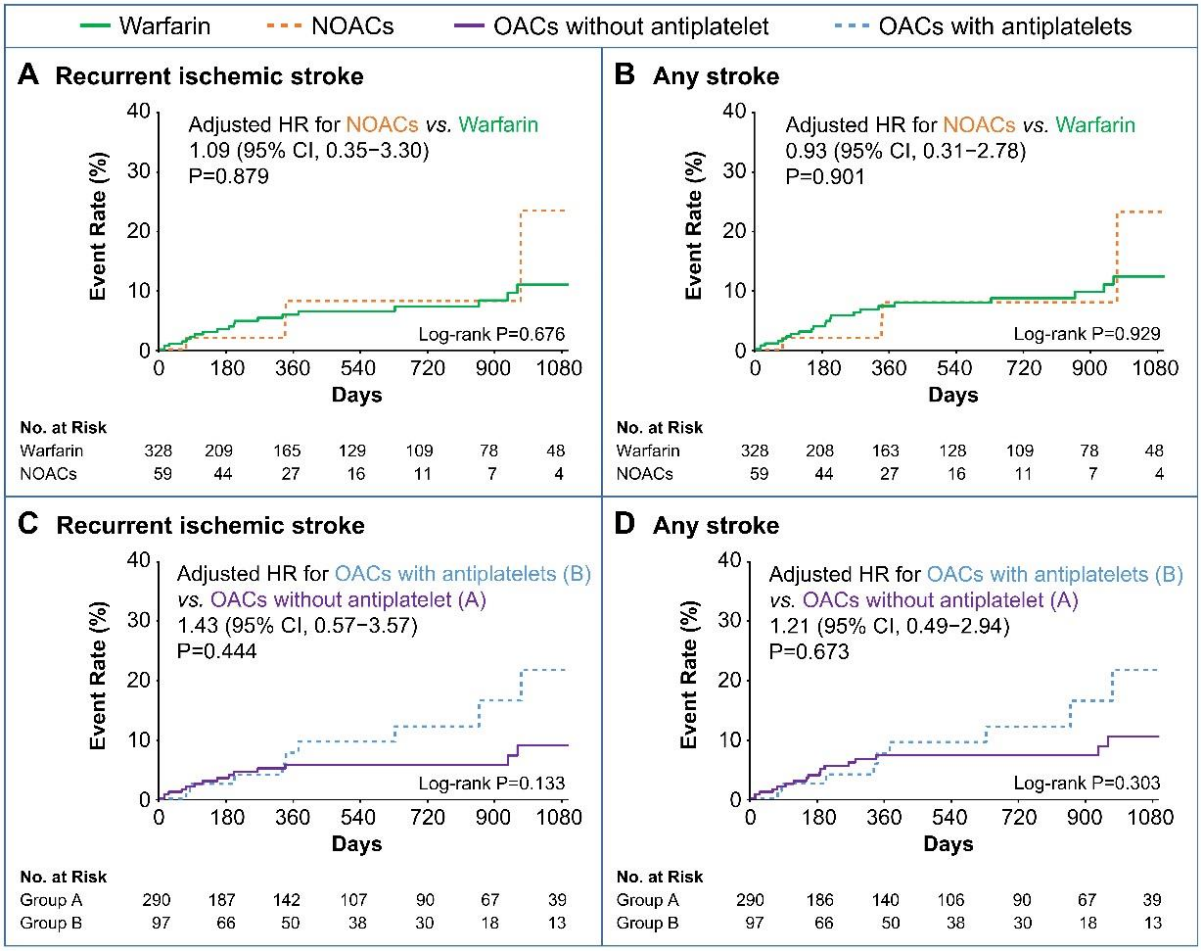

Figure S4. The cumulative incidence and adjusted hazard ratios of recurrent ischemic stroke (A and C) and any stroke (B and D) according to antithrombotic therapy in patients with D-dimer levels of ≥2.0 μg/mL. NOAC, non-vitamin K antagonist oral anticoagulants; OAC, oral anticoagulants; HR, hazard ratio; CI, confidence interval.