## ICTUS ISCHEMICO NEI PAZIENTI CON NOTA FIBRILLAZIONE ATRIALE

CORRELAZIONE TRA SEVERITÀ DELL'EVENTO E TERAPIA ANTITROMBOTICA PRECEDENTE

#### **BACKGROUND**

- Atrial fibrillation (AF) is the main cause of ischemic stroke.
- Compared with patients with ischemic stroke without AF, those with AF exhibit high stroke severity and poor outcomes.
- For patients with AF, an oral anticoagulant (OAC) is an effective medication for reducing stroke risk.
- However, in the real world, several patients with AF are still not prescribed OACs due to various reasons.

# Initial Stroke Severity in Patients With Atrial Fibrillation According to Antithrombotic Therapy Before Ischemic Stroke

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#### **METHODS**

- Data from the nationwide multicenter stroke registry
- 6786 patients with acute ischemic stroke (AIS) with known AF before stroke admission across 39 hospitals between June 2008 and December 2018.
- Data on antithrombotic medication use (no antithrombotic/antiplatelet/ anticoagulant) preceding AIS.
- Initial stroke severity was measured using the National Institutes of Health Stroke Scale, and in-hospital outcome was determined by modified Rankin Scale score at discharge.

### BASELINE CHARACTERISTICS

Variables	None	Antiplatelets	Anticoagulants	P Value*				
N	2304	2701	1781					
Preadmission factors								
Age group				0.004				
<40	10 (0.4)	9 (0.3)	8 (0.4)					
40-49	59 (2.6)	38 (1.4)	47 (2.6)					
50-59	221 (9.6)	206 (7.6)	162 (9.1)					
60–69	483 (21.0)	623 (23.1)	386 (21.7)					
70–79	864 (37.5)	1073 (39.7)	716 (40.2)					
≥80	667 (28.9)	752 (27.8)	462 (25.9)					
Mean±SD	72.8±11.0	73.1±10.0	72.3±10.5	0.027				
Female	1167 (50.7)	1327 (49.1)	966 (54.2)	0.003				
Pre-mRS				0.129				
0	1752 (76.0)	2107 (78.0)	1379 (77.5)					
1	155 (6.7)	169 (6.3)	138 (7.8)					
2	107 (4.6)	133 (4.9)	79 (4.4)					
3	106 (4.6)	131 (4.9)	80 (4.5)					
4	92 (4.0)	83 (3.1)	53 (3.0)					
5	92 (4.0)	78 (2.9)	51 (2.9)					
Hypertension	1634 (70.9)	2291 (84.8)	1399 (78.6)	<0.001				
Diabetes mellitus	654 (28.4)	840 (31.1)	591 (33.2)	0.004				
Congestive heart failure	2 (0.1)	5 (0.2)	4 (0.2)	0.512				
Hyperlipidemia	504 (21.9)	1091 (40.4)	657 (36.9)	<0.001				
Chronic kidney disease†	1236 (53.6)	1528 (56.6)	983 (55.2)	0.116				
Peripheral arterial disease	13 (0.6)	20 (0.7)	25 (1.4)	0.011				
TIA	28 (1.2)	54 (2.0)	61 (3.4)	<0.001				
Anemiat	747 (32.4)	839 (31.1)	628 (35.3)	0.013				
Severe renal diseaset	238 (10.3)	297 (11.0)	176 (9.9)	0.472				

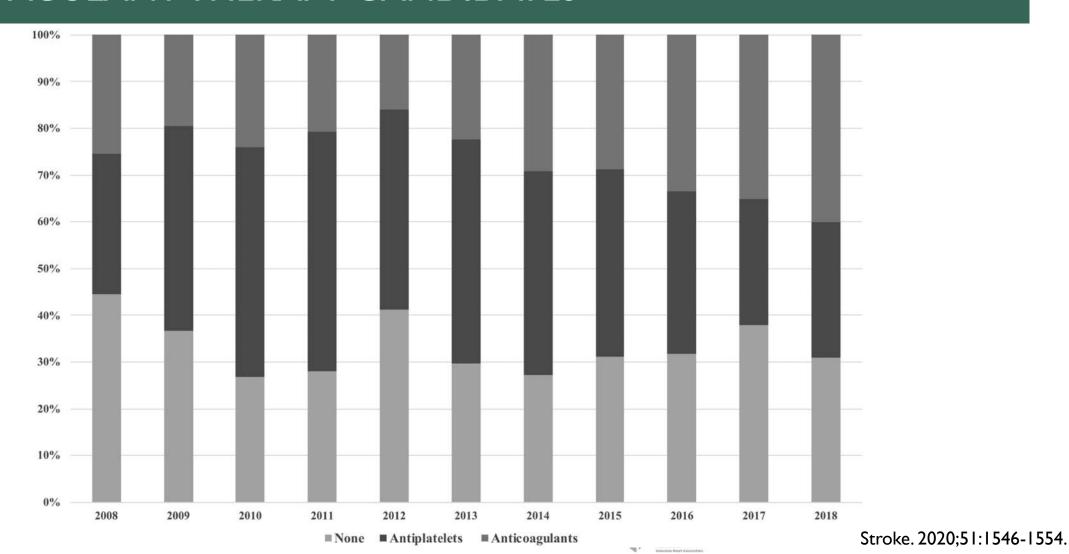
### BASELINE CHARACTERISTICS

Variables	None	Antiplatelets	Anticoagulants	P Value*
CHA <sub>2</sub> DS <sub>2</sub> -VASc score				<0.001
0	105 (4.6)	64 (2.4)	58 (3.3)	
1	330 (14.3)	316 (11.7)	208 (11.7)	
2	461 (20.0)	521 (19.3)	359 (20.2)	
3	607 (26.3)	764 (28.3)	485 (27.2)	
4	609 (26.4)	786 (29.1)	472 (26.5)	
5	191 (8.3)	247 (9.1)	194 (10.9)	
6	1 (0.0)	3 (0.1)	5 (0.3)	
Mean±SD	2.8±1.3	3.0±1.2	3.0±1.3	<0.001
Median (IQR)	3 (2-4)	3 (2-4)	3 (2-4)	<0.001
ATRIA score				<0.001
0	319 (13.8)	209 (7.7)	186 (10.4)	
1	580 (25.2)	871 (32.2)	477 (26.8)	
2	143 (6.2)	89 (3.3)	55 (3.1)	
3	506 (22.0)	636 (23.5)	442 (24.8)	
4	161 (7.0)	222 (8.2)	187 (10.5)	
5	104 (4.5)	53 (2.0)	52 (2.9)	
6	347 (15.1)	428 (15.8)	265 (14.9)	
7	23 (1.0)	43 (1.6)	23 (1.3)	
8	19 (0.8)	12 (0.4)	23 (1.3)	
9	102 (4.4)	138 (5.1)	71 (4.0)	
Mean±SD	3.0±2.4	3.1±2.4	3.1±2.4	0.241
Median (IQR)	3 (1–5)	3 (1-4)	3 (1–4)	0.060
Treatment, acute thrombolytic				<0.001
No	1584 (70.2)	1829 (68.9)	1281 (72.4)	
IV tPA	321 (14.2)	416 (15.7)	182 (10.3)	
IA	149 (6.6)	171 (6.4)	184 (10.4)	
IV tPA+IA	202 (9.0)	239 (9.0)	123 (6.9)	

### PREADMISSION ANTITHROMBOTIC THERAPY IN ORAL ANTICOAGULANT THERAPY CANDIDATES

	Years												
Treatment	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total	P Valuet
Anticoagulants	29 (25.0)	49 (19.4)	83 (25.0)	68 (19.1)	72 (16.6)	96 (22.2)	111 (28.1)	128 (27.6)	129 (32.7)	128 (34.9)	189 (40.6)	1,082 (27.0)	<0.001
NOAC	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	9 (2.1)	3 (0.8)	20 (4.3)	56 (14.2)	80 (21.8)	117 (25.1)	286 (7.1)	
Antiplatelets	35 (30.2)	114 (45.1)	163 (49.1)	186 (52.2)	190 (43.9)	204 (47.2)	181 (45.8)	187 (40.3)	142 (35.9)	104 (28.3)	143 (30.7)	1,649 (41.1)	<0.001
None	52 (44.8)	90 (35.6)	86 (25.9)	102 (28.7)	171 (39.5)	132 (30.6)	103 (26.1)	149 (32.1)	124 (31.4)	135 (36.8)	134 (28.8)	1,278 (31.9)	0.290
Total	116	253	332	356	433	432	395	464	395	367	466	4,009	

### PREADMISSION ANTITHROMBOTIC THERAPY IN ORAL ANTICOAGULANT THERAPY CANDIDATES



#### SEVERITY OF NEUROLOGICAL DEFICIT AND FUNCTIONAL OUTCOMES BASED ON ANTITHROMBOTIC USE BEFORE STROKE EVENT

Variables	None	Antiplatelets	Anticoagulants	P Value*	<i>P</i> ª†	<i>P</i> ⁵†	<i>P</i> °†	
N	2304	2701	1781					
Severity of neurological deficits	Severity of neurological deficits							
NIHSS score at admission, median (IQR)	8 (3–15)	7 (2–15)	6 (2–14)	<0.001	<0.001	<0.001	0.776	
NIHSS score at discharge, median (IQR)	4 (1–12)	3 (1–11)	3 (1–10)	<0.001	<0.001	<0.001	0.852	
mRS score at discharge				<0.001	<0.001	<0.001	>0.999	
Favorable (mRS score 0-2)	970 (42.8)	1,332 (50.9)	883 (50.6)					
Nonfavorable (mRS score 3-6)	1,294 (57.2)	1,287 (49.1)	862 (49.4)					
Mortality	167 (7.4)	157 (6.0)	133 (7.6)	0.062	0.159	>0.999	0.105	

### INDEPENDENT PREDICTORS OF MILD SEVERITY OF ISCHEMIC STROKE IN PATIENTS WITH ATRIAL FIBRILLATION

	Univariate Ana	alysis	Multivariable Analysis*					
Risk Factors	Odds Ratio (95% CI) P Value		Odds Ratio (95% CI)	P Value				
Antithrombotics at admission								
None	Ref		Ref					
Antiplatelets	1.22 (1.09-1.37)	0.001	1.16 (1.03–1.31)	0.015				
Anticoagulation	1.29 (1.14–1.47)	<0.001	1.25 (1.10–1.43)	0.008				
Age, per 10 y	0.71 (0.68-0.75)	<0.001	0.81 (0.76-0.85)	<0.001				
Female sex	0.52 (0.47-0.58)	<0.001	0.67 (0.60-0.77)	<0.001				
Pre-mRS	0.73 (0.70-0.77)	<0.001	0.78 (0.74-0.81)	<0.001				
Congestive heart failure	1.25 (0.38-4.11)	0.7107						
Chronic kidney disease	0.64 (0.58-0.71)	<0.001	0.98 (0.87-1.11)	0.780				
Diabetes mellitus	1.00 (0.90-1.11)	0.955						
Hypertension	0.94 (0.84–1.06)	0.306						
Smoking	1.63 (1.46-1.83)	<0.001	1.09 (0.96–1.24)	0.193				
Hyperlipidemia	1.31 (1.18–1.45)	<0.001	1.24 (1.11–1.38)	0.001				
TIA	1.54 (1.10-2.14)	0.011	1.45 (1.02-2.04)	0.036				
Anemia	0.60 (0.54-0.67)	<0.001	0.89 (0.79-1.01)	0.060				
Severe renal disease	0.54 (0.45-0.64)	<0.001	0.83 (0.68-1.00)	0.050				

#### LIMITATIONS

- Retrospective observational analysis.
- No data on the previous history of stroke (ischemic or hemorrhagic), except TIA, falling, and hemorrhagic complications, which could be a reason for not using antithrombotics.
- Unknown initial INR levels of patients taking anticoagulants and the doses of NOACs
- Missing values of NIHSS scores (2.1%) and mRS scores at discharge (2.3%).

#### **CONCLUSIONS**

- During the study period, there was an increase in pre-stroke OAC use, whereas antiplatelet use decreased in patients with AIS with AF.
- Although preceding OAC use increased after the introduction of NOACs in clinical practice, several patients with AIS with known AF did not take OACs.
- The preventive use of OACs in patients with AIS with AF was associated with a significant higher likelihood of a mild initial neurological deficit and favorable outcome at discharge.