Stroke

ORIGINAL CONTRIBUTION

Safety of Anticoagulation in Patients Treated With Urgent Reperfusion for Ischemic Stroke Related to Atrial Fibrillation

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BACKGROUND AND PURPOSE: The optimal timing for starting oral anticoagulant after an ischemic stroke related to atrial fibrillation remains a challenge, mainly in patients treated with systemic thrombolysis or mechanical thrombectomy. We aimed at assessing the incidence of early recurrence and major bleeding in patients with acute ischemic stroke and atrial fibrillation treated with thrombolytic therapy and/or thrombectomy, who then received oral anticoagulants for secondary prevention.

METHODS: We combined the dataset of the RAF and the RAF-NOACs (Early Recurrence and Major Bleeding in Patients With Acute Ischemic Stroke and Atrial Fibrillation Treated With Non–Vitamin K Oral Anticoagulants) studies, which were prospective observational studies carried out from January 2012 to March 2014 and April 2014 to June 2016, respectively. We included consecutive patients with acute ischemic stroke and atrial fibrillation treated with either vitamin K antagonists or nonvitamin K oral anticoagulants. Primary outcome was the composite of stroke, transient ischemic attack, symptomatic systemic embolism, symptomatic cerebral bleeding, and major extracerebral bleeding within 90 days from the inclusion. Treated-patients were propensity matched to untreated-patients in a 1:1 ratio after stratification by baseline clinical features.

RESULTS: A total of 2159 patients were included, 564 (26%) patients received acute reperfusion therapies. After the index event, 505 (90%) patients treated with acute reperfusion therapies and 1287 of 1595 (81%) patients untreated started oral anticoagulation. Timing of starting oral anticoagulant was similar in reperfusion-treated and untreated patients (median 7.5 versus 7.0 days, respectively). At 90 days, the primary study outcome occurred in 37 (7%) patients treated with reperfusion

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Lesion <1.5 cm	154 (27%)	666 (42%)	<0.001
NIHSS at admission, median (IQR)	10.0 (10)	4.0 (7)	<0.001
Treatment			
Resumption of oral anticoagulation	505 (90%)	1287 (81%)	0.147
NOAC	384 (76%)	841 (65%)	<0.001
Warfarin	121 (22%)	446 (28%)	<0.001
Starting anticoagulation time (d), median (IQR)	7.5 (10)	7 (11)	0.287

AF indicates atrial fibrillation; IA, intra-arterial thrombectomy; IQR, interquartile range; NIHSS, National Institutes of Health; NOAC, nonvitamin K oral anticoagulant; and r-tPA, recombinant tissue-type plasminogen activator.

Table 1. Main Characteristics of the Study Patients

Overall Patients, 2159	r-tPA/IA, 564 (26%)	No Reperfusion Therapies; 1595 (74%)	*P* Value
Demographics			
Age	74.54±10.1	76.96±9.6	<0.001
Female	260 (46%)	735 (46%)	0.961
Risk factors			
Diabetes mellitus	94 (17%)	388 (24%)	<0.001
Hypertension	431 (77%)	1258 (79%)	0.171
Hyperlipidemia	184 (33%)	540 (34%)	0.640
Paroxysmal AF	284 (50%)	646 (41%)	<0.001
Previous stroke	104 (19%)	464 (29%)	0.001
Current smoking	50 (9%)	156 (10%)	0.560
Alcoholism	30 (5%)	112 (7%)	0.198
Chronic heart failure	84 (15%)	285 (18%)	0.118
Previous MI	68 (12%)	231 (15%)	0.157
Peripheral arterial disease	39 (7%)	143 (9%)	0.135
Aortic atheroma	44 (8%)	123 (8%)	0.711
Pacemaker	36 (6%)	114 (7%)	0.630
CHA_2DS_2-VASc ≥5	406 (72%)	1264 (79%)	0.0001
Clinical and radiological characteristics			

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Table 2. Rate of Primary and Secondary Study Outcomes in Patients Treated or Untreated With Acute Reperfusion Therapies

Overall; 2159	r-tPA/IA; 564 (26%)	No Reperfusion Therapies; 1595 (74%)	Odds Ratio (95% CI)
Primary outcome			
Any ischemic and any hemorrhagic event	37 (7%)	139 (9%)	Unadjusted OR, 0.74; 95% CI, 0.50–1.07
			Adjusted OR, 0.85; 95% CI, 0.53–1.36
Secondary outcomes			
Any ischemic event	24 (4%)	82 (5%)	Unadjusted OR, 0.82; 95% CI, 0.51–1.31
			Adjusted OR, 1.01; 95% CI, 0.56–1.72
Any hemorrhagic event	13 (2%)	64 (4%)	Unadjusted OR, 0.56; 95% CI, 0.31–1.03
			Adjusted OR, 0.60; 95% CI, 0.29–1.26
Mortality	26 (4%)	111 (7%)	Unadjusted OR, 0.65; 95% CI, 0.42–1.00
			Adjusted OR, 0.47; 95% CI, 0.29–0.78
Disability (mRS 3–5)	182 (32%)	492 (31%)	Unadjusted OR, 1.07; 95% CI, 0.87–1.31
HT 24–72	63 (11.2%)	176 (11%)	Unadjusted OR, 1.01; 95% CI, 0.75–1.38

HT indicates hemorrhagic transformation; IA, intra-arterial thrombectomy; mRS, modified Rankin Scale; OR, odds ratio; and r-tPA, recombinant tissue-type plasminogen activator.

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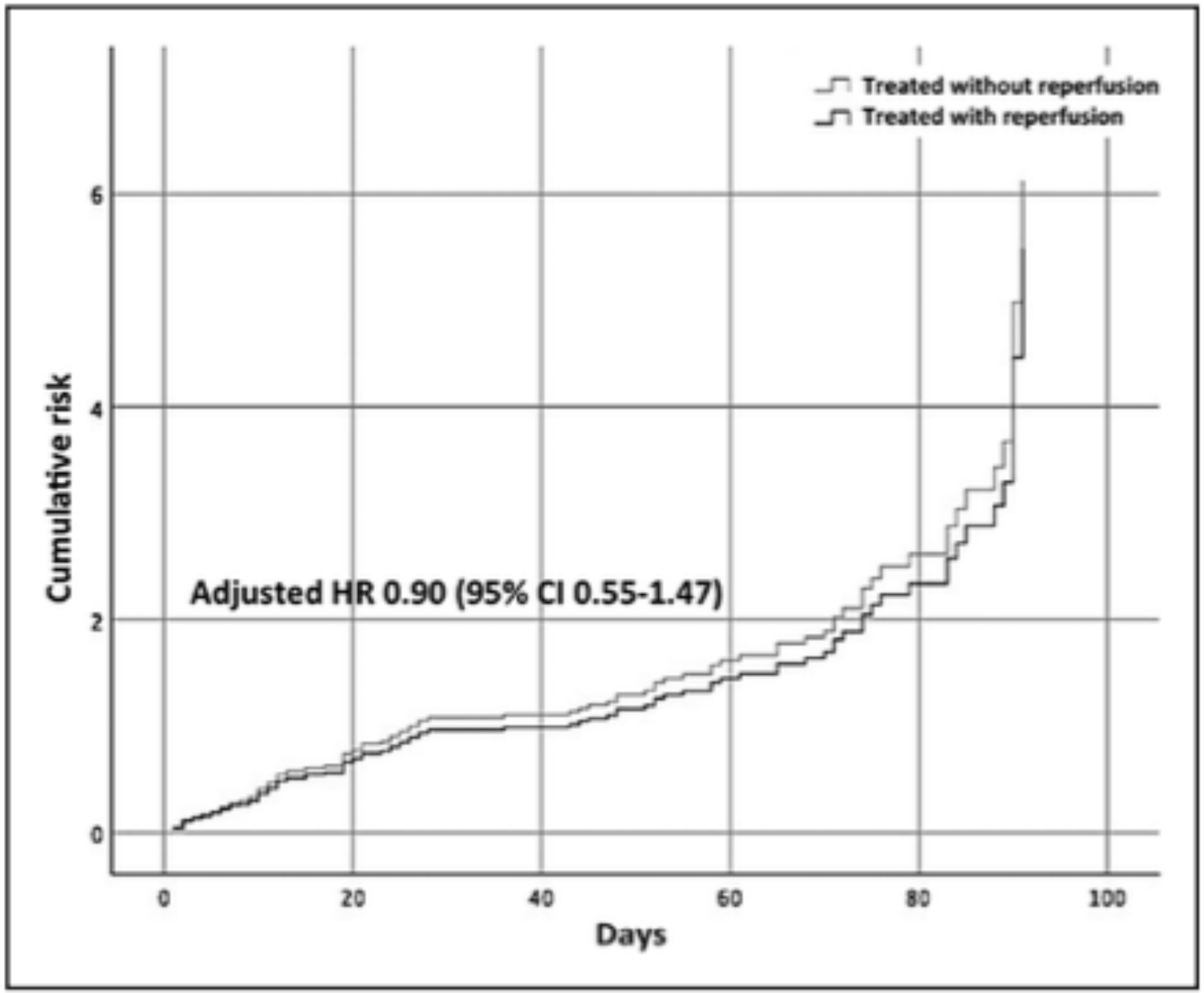

Figure. Cumulative risk of the primary study outcome.

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Table 3. Multivariate Analysis of the Primary Outcome and of Any Ischemic and Any Hemorrhagic Event

	OR	95% CI	*P* Value
Primary outcome			
Paroxysmal AF	0.77	0.51–1.11	0.212
Lesion <1.5 cm	0.57	0.37–0.87	0.008
Current smoker	0.74	0.33–1.64	0.454
r-tPA/IA	0.87	0.55–1.38	0.556
CHA_2DS_2-VASc	1.24	1.06–1.44	0.006
NOACs vs VKAs	0.44	0.29–0.65	<0.001
Any ischemic event			
Paroxysmal AF	0.66	0.39–1.12	0.125
Lesion <1.5 cm	0.70	0.49–2.85	0.183
Current smoker	0.72	0.33–1.64	0.454
r-tPA/IA	0.98	0.55–1.76	0.961
CHA_2DS_2-VASc	1.29	1.07–1.56	0.008
NOACs vs VKAs	0.40	0.24–0.66	<0.001
Any hemorrhagic event			
Paroxysmal AF	0.97	0.53–1.78	0.922
Lesion <1.5 cm	0.43	0.22–0.84	0.013
Current smoker	0.21	0.03–1.54	0.125
r-tPA/IA	0.67	0.32–1.38	0.274
CHA_2DS_2-VASc	1.11	0.88–1.39	0.379
NOACs vs VKAs	0.52	0.29–0.95	0.033

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Table 4. Characteristics of the Patients After Propensity Score Matching

	r-tPA/IA (n=304)	No Reperfusion Therapies (n=304)	*P* Value
Age (y, mean)	75.6±9.4	75.1±9.7	0.5
Female sex	165 (54.3%)	157 (51.6%)	0.6
NIHSS at admission (mean)	8.9±5.0	8.3±6.9	0.2
Diabetes mellitus	65 (21.4%)	53 (17.4%)	0.3
Hypertension	235 (77.3%)	234 (77.0%)	1.0
Dyslipidemia	96 (31.6%)	96 (31.6%)	1.0
Paroxysmal AF	146 (48.0%)	147 (48.4%)	1.0
Current smoker	26 (8.6%)	27 (8.9%)	1.0
History of stroke/TIA	76 (25.0%)	65 (21.4%)	0.3
History of CHF	45 (14.8%)	54 (17.8%)	0.4
Use of oral anticoagulant	251 (82.6%)	258 (84.9%)	0.5
Use of LMWH (with/without bridging)	65 (21.5%)	78 (25.5%)	0.2

AF indicates atrial fibrillation; IA, intra-arterial thrombectomy; LMWH, low-molecular weight-heparin; NIHSS, National Institutes of Health Stroke Scale; r-tPA, recombinant tissue-type plasminogen activator; and TIA, transient ischemic attack.

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Table 5. Risks of Primary and Secondary Outcome After Propensity Score Matching Between Patients Treated With or Without Acute Reperfusion Therapies

	r-tPA/IA (n=304)	No Reperfusion Therapies (n=304)	Odds Ratio (95% CI)	*P* Value
Primary outcome	20 (6.6%)	19 (6.3%)	1.06 (95% CI, 0.53–2.02)	0.9
Any ischemic event	13 (4.3%)	11 (3.6%)	1.19 (95% CI, 0.52–2.70)	0.7
Any hemorrhagic event	7 (2.3%)	10 (3.3%)	0.69 (95% CI, 0.26–1.84)	0.6

IA indicates intra-arterial thrombectomy; and r-tPA= recombinant tissue-type plasminogen activator.

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CONCLUSIONS

In conclusion, our study suggests that acute reperfusion therapies seem not to influence the risk of early recurrence and major bleeding in patients with AF-related acute ischemic stroke, who subsequently started oral anticoagulant treatment. Therefore, acute reperfusion treatment should not refrain stroke physicians from an early initiation of oral anticoagulation for secondary stroke prevention when the potential benefits outweigh the perceived risks. Further studies, preferably randomized trials, are needed to better investigate this issue.

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