Acute Ischemic Stroke in Patients on Treatment with Non-Vitamin K oral Anticoagulants: Safety and Efficacy of NOAC Plasma-Level-Guided Therapy

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BACKGROUND: The management of patients with acute ischemic stroke during treatment with non-vitamin K oral anticoagulants (NOAC) is challenging. Functional NOAC-plasma-levels could guide decisions on therapies.

METHODS: A standard operating procedure for patients on NOAC was established: Patients with a plasma level below 50 ng/mL were considered eligible for intravenous thrombolysis (IVT), while levels above 100 ng/mL constituted an exclusion criterion. Levels between 50 to 100 ng/mL allowed an individual decision (Figure 1). For patients on vitamin-K antagonists (VKA), a cutoff for IVT was set at INR 1.7. Mechanical recanalization (EVT) of a large vessel occlusion was indicated independently from coagulation testing. Consecutive patients were included in an observational registry starting in January 2014.

Figure 1: Standard operating procedure (SOP) for intravenous thrombolysis in acute ischemic stroke for patients on non-vitamin K oral anticoagulants (NOAC).

¹Patients on Dabigatran alternatively receive Idarucizumab (since available) to be considered eligible for IVT.

RESULTS: 523 patients (262 on NOAC and 261 on VKA) were included. Patients were on treatment with Apixaban (131), Rivaroxaban (85), Dabigatran (37), Edoxaban (9) or Phenprocoumon (261) within 48 hours prior to admission. The functional NOAC-plasma level was assessed in a total of 207 (79.0%) patients (Figure 2 and 3).

47 (18.0%) of the VKA patients and 42 (16.0%) of the NOAC patients underwent a recanalization therapy with IVT and/or EVT according to the standard operating procedure. Among the patients under VKA, 30 received IVT and 27 underwent EVT, including 10 who received both. 24 of the NOAC patients received IVT, 31 underwent EVT and 14 both. Successful mechanical recanalization (TICI 2b-3) was achieved in 23 (85.2%) VKA patients and 28 (90.3%) NOAC patients. There were **no differences in rates of major intracranial hemorrhage, which occurred in 2 (4.3%) VKA and 2 (4.8%) NOAC patients; $P=0.908$** . 11 (25.0%) patients on VKA and 17 (41.5%) patients on NOAC had a favorable outcome (mRS 0-2); $P=0.107$ (Figure 4).

CONCLUSION: The assessment of functional NOAC-plasma levels is feasible to support decisions on recanalization therapies. Under consideration of defined thresholds, no higher bleeding rates after treatment were observed when compared to established guidelines for patients under VKA.

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Figure 2: Oral anticoagulation on admission. The NOAC group is further divided into a reduced (red.) and maximum (max.) daily NOAC-dose.

Figure 3: NOAC-Plasma-Level on admission.

	VKA (n=47)	NOAC (n=42)	PValue
Age (years)	80 (74-83)	77 (73-83)	0.367
Atrial fibrillation	42 (89.4%)	38 (90.5%)	0.862
Admission ≤ 4.5 hrs	36 (76.6%)	31 (73.8%)	0.761
Large vessel occlusion	39 (83.0%)	37 (88.1%)	0.495
Coagulation			
Phenprocoumon	47 (100%)	-	
Apixaban	-	18 (42.9%)	
Rivaroxaban	-	15 (35.7%)	
Dabigatran	-	8 (19.0%)	
Edoxaban	-	1 (2.4%)	
NOAC max. daily dose	-	20 (47.6%)	

Table 1: Baseline characteristics of the IVT/EVT subgroup; number (%) or median (IQR).

	VKA (n=47)		NOAC (n=42)			
	INR		Drug-specific plasma-level [ng/mL]			
	≤1.7 (n=36)	>1.7 (n=11)	<50 (n=23)	50-100 (n=11)	>100 (n=6)	N/A (n=2)
IVT	29	1	21	3	0	1
EVT	17	10	14	9	6	2
IVT+EVT	10	0	12	1	0	1
TICI 2b-3	15	8	12	8	6	2
ICH _{any}	6	7	5	3	0	0
sICH _{ECASS}	1	1	1	1	0	0

Table 2: IVT/EVT subgroup. The number of patients which underwent a recanalization therapy, recanalization numbers and the number of intracranial hemorrhage are displayed.

Figure 4: mRS at 3 months in the IVT/EVT subgroup.