SUPPLEMENTAL MATERIAL

Intravenous Thrombolysis With Alteplase at 0.6 mg/kg in Patients With Ischemic Stroke Taking Direct Oral Anticoagulants

Table S1. Regimens of direct oral anticoagulants before stroke onset

Oral anticoagulants	n
Dabigatran 150 mg BID	3
Dabigatran 110 mg BID	3
Rivaroxaban 10 mg QD	8
Apixaban 10 mg BID	9
Apixaban 5 mg BID	7
Edoxaban 60 mg QD	1
Edoxaban 30 mg QD	7
Edoxaban 15 mg QD	2

Data are presented as number of patients. BID, bis in die (twice a day); QD, quaque die (once a day).

Table S2. Baseline characteristics of patients on DOACs who developed hemorrhagic events after administration of intravenous alteplase

Cases	DOACs	Dose (mg/ day)	Duration from last intake to stroke IVT (hours)	Age (years)	Sex	BW (kg)	CCr (mL/min)	PT-INR	APTT (seconds)	Baseline NIHSS score	LVO	EVT	Combination of antiplatelet agents	Hemorrhagic events	mRS at 3 months
Any ICH															
Symptomatic ICH															
1	Rivaroxaban	10	About 8	88	M	55	31.0	1.20	29	32	ICA	-	-	PH 2	6
Other ICH															
2	Apixaban	5	12–24	87	M	57	28.9	1.19	32	28	MCA M1	-	-	HI 1	5
3	Edoxaban	30	12–24	91	F	44	22.7	1.12	30	17	MCA M2	+	Clopidogrel	HI 1	4
4	Rivaroxaban	10	12–24	87	M	61	38.1	1.19	31	5	MCA M1	+	-	HI 1, SAH	0
5	Rivaroxaban	10	12–24	75	M	60	52.6	1.03	29	28	MCA M2	+	-	HI 2, SAH	4
Hemorrhagic events fulfilling ISTH criteria															
6	Rivaroxaban	10	12–24	83	M	68	79.2	1.45	23	14	MCA M1	+	-	Bleeding at vascular access site	3

APTT, activated partial thromboplastin time; BW, body weight; CCr, creatinine clearance (calculated by Cockcroft–Gault equation); DOAC, direct oral anticoagulant; EVT, endovascular therapy; F, female; HI, hemorrhagic infarction; ICA, internal carotid artery; ICH, intracranial hemorrhage; ISTH, International Society on Thrombosis and Haemostasis; IVT, intravenous thrombolysis; LVO, large vessel occlusion; mRS,

modified Rankin Scale; M, male; MCA, middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; PH, parenchymal hematoma; PT-INR, prothrombin time–international normalized ratio; SAH, subarachnoid hemorrhage.

Table S3. Reasons for non-administration of alteplase for patients on DOACs

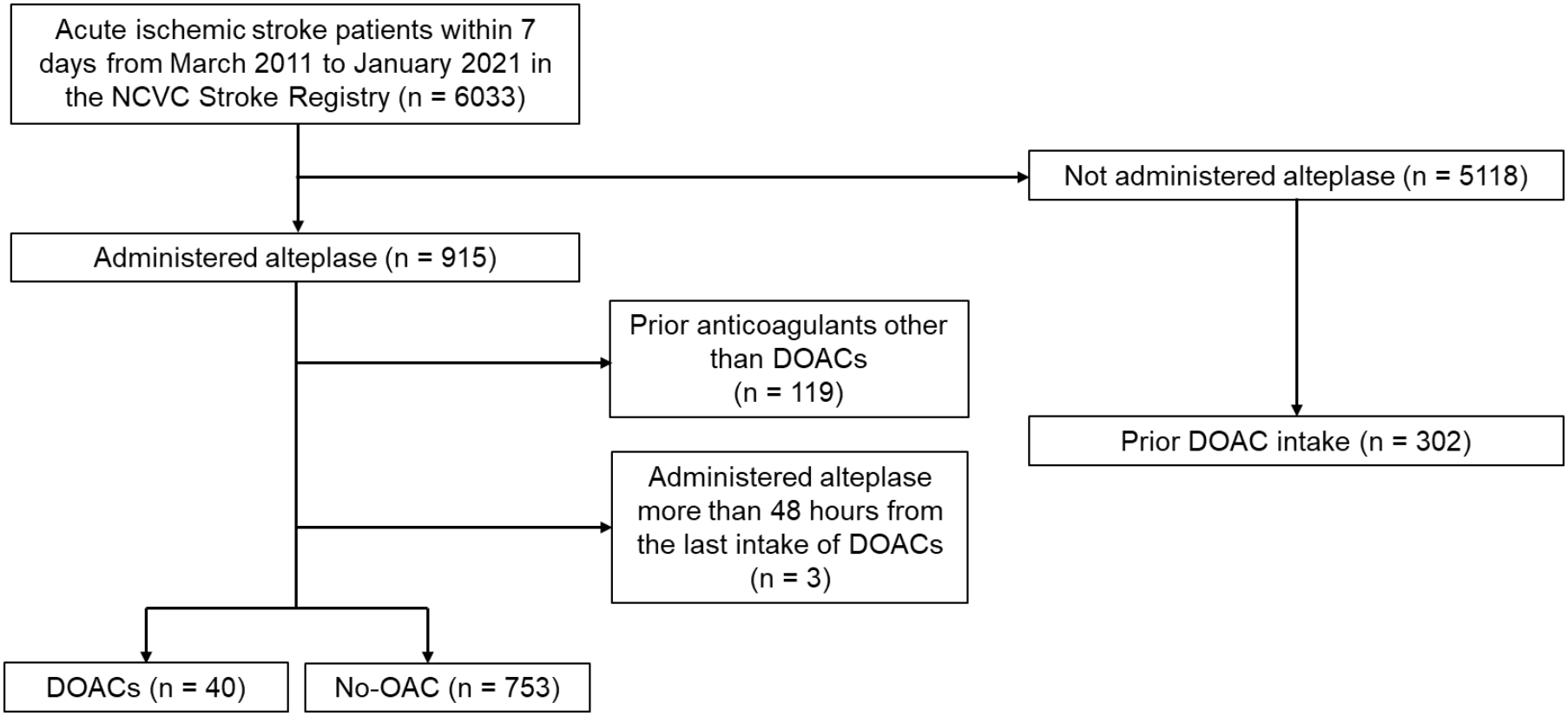
Reasons	n
Total	302
Outside the time window for IVT*	204
Reason other than outside of the time window†	98
Mild neurological symptom or rapid symptom improvement	58
Extensive infarct on baseline imaging	17
PT-INR of >1.7 or APTT of >40 seconds	9
Previous intracranial hemorrhage	8
Recent ischemic stroke	8
Onset immediately after DOAC intake	4
Consent not obtained for religious reasons	2
Suspicious of other disease on admission	2
Recent surgery	1
History of gastrointestinal bleeding (remote) or genitourinary bleeding	1
Severe liver damage	1

APTT, activated partial thromboplastin time; DOAC, direct oral anticoagulant; IVT, intravenous thrombolysis; PT-INR, prothrombin time–international normalized ratio.

* "Outside the time window for IVT" indicated patients who arrived at our hospital more than 4.5 hours from stroke onset or the last known well time.

†Multiple reasons per patient allowed.

Figure S1. Flow chart of patient selection in the present study



DOAC, direct oral anticoagulant; IVT, intravenous thrombolysis; OAC, oral anticoagulant; NCVC, National Cerebral and Cardiovascular Center; VKA, vitamin K antagonist