Clinical characteristics of intracranial hemorrhages in patients treated with direct oral anticoagulants in secondary stroke prevention

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Background and Aims

Risk of hemorrhagic complications in patients anticoagulated after a cardioembolic stroke is double than in primary prevention. Direct oral anticoagulants (DOACs) reduce the risk of intracranial hemorrhage (ICH) by 50% compared to warfarin. We present our clinical experience of ICH secondary to DOACs in secondary prevention.

Method

We performed an observational, retrospective study of anticoagulated patients with DOACs in secondary prevention of stroke from October 2010 to June 2015 at our center. Clinical, radiological and ICH variables were collected.

Results

We included 425 patients (women, 53.4%; mean age 77.1 ± 10.2 yo). 40 patients were lost during follow-up. There were no differences in clinical variables (Table 1). DOAC distribution is detailed in Fig 1. Patients in treatment with Dabigatran has more prolonged follow-up due to its earlier commercialization (mean follow-up: Dabigatran 29.0 months; Rivaroxaban 25.0 months, Apixaban 15.5 months). Median CHA2DS2-VASc was 5 (range 2 - 8) and HAS-BLED was 2 (range 1 - 4).

Table 1: Clinical variables			
	No ICH N 375	ICH N 10	p (χ²)
Age	77,1±10,2 yo	82,5±7,9 yo	0,62
Hypertension	79%	60%	0,14
Diabetes	26,1%	30%	0,78
Dyslipidemia	43,9%	40%	0,79
Chronic kidney disease	5%	10%	0,49
Previous ICH	8,3%	20%	0,19
Myocardial infarction	11,5%	10%	0,88
Peripheral arteriopathy	5,7%	10%	0,57

Fig 1: Distribution of patients by DOAC and dose (up) and by year (bottom)

During follow-up there were 10 ICH (0.015 cases/person-year), median of 36 months (7-78) from the beginning of treatment. Patients were receiving treatment with Dabigatran (8), Apixaban (1) and Rivaroxaban (1). There were 5 spontaneous intraparenchymal hematomas, 3 post-traumatic subarachnoid hemorrhage, an intraventricular hemorrhage and a subdural hematoma. Anticoagulation was reversed in 3 cases. Long-term secondary stroke prevention is shown in Table 2.

Table 2: Long-term secondary stroke prevention	
ACOD discontinuation	4 patients (intraparenchymal hemorrhages) 1 left atrial appendage closure
ACOD continuation	4 patients 3 post-traumatic SAH 1 post-traumatic subdural haematoma

There were 2 deaths related to ICH. At 3 months 70% presented mRS ≤ 2 (Figure 2).

Fig 2: Basal modified Rankin Score (up) and at 3 months (bottom)

Conclusions

The rate of ICH in patients with DOACs in secondary stroke prevention was similar to that of the pivotal studies and patients presented low disability at 3 months.

References

1. Ruff CT, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet 2014;383(9921):955-62.
2. Wilson D, et al. Outcome of intracerebral hemorrhage associated with different oral anticoagulants. Neurology 2017; 88:1693-1700.
3. Ntaios G, et al. Nonvitamin-K-antagonist oral anticoagulants versus warfarin in patients with atrial fibrillation and previous stroke or transient ischemic attack: An updated systematic review and meta-analysis of randomized controlled trials. Int J Stroke. 2017; 12: 589-596