

Concordance between guidelines on perioperative management of Novel Oral Anticoagulants and its implementation and preventable causes of the occurrence of ischaemic stroke

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BACKGROUND & AIM

Increasing numbers of patients receiving a NOAC are undergoing elective surgery. The extent to which **perioperative interruption of NOAC therapy** are concordant with best evidence is uncertain. A minority of the patients develops in the perioperative period (-5dy till 2dy) an **ischaemic stroke**.

This **study** investigates whether a possibly inappropriate peri-operative advice can lead to the occurrence of an ischaemic stroke. Concordance with European Heart Rhythm Association (EHRA) guidelines will be analysed. Further, we examined the relation to inappropriate dosing, peri-operative management, pharmacodynamics and pharmacokinetic interactions.

METHODS

Data from all ischaemic stroke patients, prior treated with a NOAC, were retrospectively collected from the EVAS-BE-database (01/2019-10/2019). This is a single center database of all admitted stroke patients in AZ Groeninge hospital (Kortrijk). The following data were retrieved from the electronic patient files: date of stroke, etiology, previous ischaemic/haemorrhagic stroke, posology & indication NOAC, renal function (GFR), weight, age, concomitant drugs, surgery (indication, date, bleeding risk, preoperative advice, advice in accordance with regional and EHRA guidelines), medication management post-stroke and discharge therapy. Concordance of perioperative anticoagulation management with regional and EHRA guidelines was rated by a clinical pharmacist according to explicit thrombosis and bleeding risk.

RESULTS

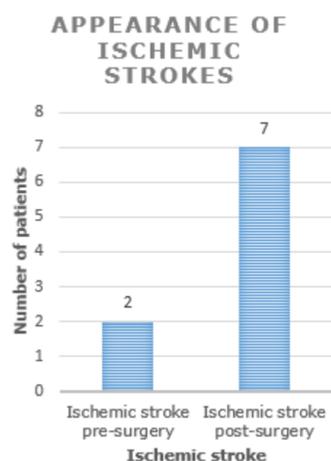
Of the 57 included patients with an ischaemic stroke under NOAC, nine patients (16%) were planned to undergo surgery. In 2 patients (3,5%) the ischaemic stroke appeared before surgery and in 7 patients (12,3%) post surgery (Fig.1). The decision to interrupt anticoagulation was concordant with regional guidelines. A minor (**M**) bleeding risk was seen in 45%, low (**L**) risk 33% and high (**H**) risk 22% (Fig.2). On the other hand, compared to EHRA guidelines: three cases stopped without indication (5dy-2dy), three light and one high bleeding risk patient stopped too early (Fig.3). None of them were bridged.

Of the 57 included patients, NOAC treatment was indicated for : atrial fibrillation (95%), pulmonary embolism (3.5%) and one unknown indication. First of all **inappropriately dosing** (30%) and **posology** (7%) based on the SmPC criteria for renal function, weight and age was identified. Of the 17 inappropriately dosed patients, underdosing was mainly the driving factor (16 vs. 1). Table 1 shows the different reasons for underdosing (renal function, weight, age, a combination or an unknown reason).

Reason underdosing	Apixaban	Edoxaban	Dabigatran	Rivaroxaban
Renal function		1	1	3
Weight			1	
Age			1	
Renal function, weight and age	1			
Renal function and weight	3	4		
Renal function and age			1	
Unknown reason				1
TOTAL (n; %)	4 (25%)	5 (31%)	3 (19%)	4 (25%)

Table 1: Reason underdosing based on the SmPC criteria

Secondly, 16 patients (28%) showed one or more **interactions** (pharmacodynamic or pharmacokinetic) with concomitant drug (Fig. 4). Due to the pharmacodynamic interactions; a higher thrombosis risk was seen in 2 patients and higher bleeding risk in 11 patients. Four patients showed a pharmacokinetic interaction; three off them were an increased effect of the NOAC and one of them were an decreased effect. Additionally there was an 'unknown effect' due to the interaction by six patients according to the EHRA guidelines. Simultaneous treatment with antiplatelet therapy was detected in 6 patients (11%). Thirdly, greatest risk in the peri-operative phase seemed to be post-surgery in comparison with pre-surgery; respectively seen in 7 and 2 patients. And finally, medication adherence could be questioned in 5 patients (9%).



SURGICAL BLEEDING RISK

- Minor risk (cfr. EHRA): Biopsy skin at eyelid, Tooth extraction(2), Colonoscopy
- Low risk (cfr. EHRA): Biopsy chest, Pacemaker implantation, ERCP with stenting
- High risk (cfr. EHRA): Lumbal facet infiltration; Hernia repair

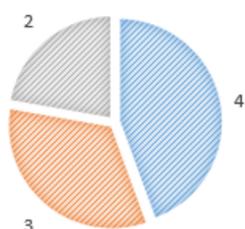


Figure 1: Appearance of ischemic strokes Figure 2: Surgical bleeding risk

NOAC	Bleeding risk + surgery	Pre-operative advice	EHRA guidelines
Rivaroxaban	M : biopsy skin at eyelid	Stop 2 days	No need to stop
Apixaban	M : tooth extraction	Stop 4 - 5 days	No need to stop
Edoxaban	M : tooth extraction	Stop 2 days	No need to stop
Dabigatran	L : biopsy chest	Stop 3 - 4 days	Stop 1 day
Edoxaban	L : pacemaker implantation	Stop 5 days	Stop 1 day
Dabigatran	L : ERCP with stenting	Stop 2 days	Stop 1 day
Rivaroxaban	H : hernia repair	Stop 5 days	stop 2 days

Figure 3: Pre-operative advice

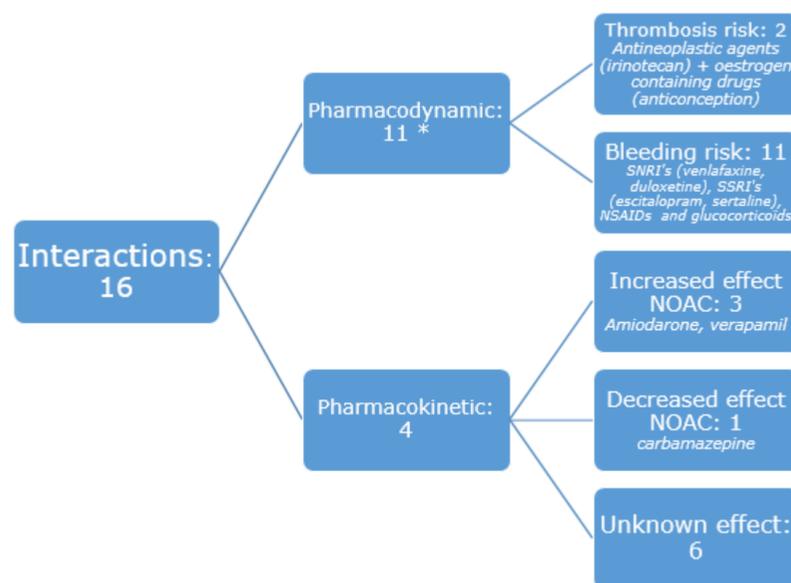


Figure 4: Interaction types
*: one patient with a double interaction

CONCLUSION

Occurrence of ischaemic stroke in the peri-operative phase in patients treated with NOAC is a major problem. Main issue seems the **discordance between our regional and EHRA guideline regarding perioperative NOAC management**. Beside the perioperative transition phase (in particular post-surgery), other main reasons for its occurrence are **inappropriate dosing, drug-interactions and non-compliance**.