ClotPro

ClotPro® DOAC assays

Exclusion of DOAC activity within 5 min

DOACs are increasingly used.

Metabolization (dabigatran) and renal function affect DOAC drug half-life and efficacy (fig. 1). Drug interaction, compliance, patient age and specific clinical conditions may alter pharmacodynamics and drug activity.

Routine monitoring of DOACs isn't required, but in several situations a rapid DOAC detection is desirable, e.g. in major trauma or ischemic stroke to aid therapeutic decisions.

Dedicated assays (anti-Xa and diluted thrombin time) are the reference methods for DOACs, but not available in many centers.

Routine global assays (PT, aPTT) detect DOACs at higher concentrations but are less useful at lower activities (and useless for apixaban).

Stroke patients on DOAC therapy

"In acute ischaemic stroke, the benefit of thrombolysis is highly time-dependent but there are many barriers in obtaining the (plasma DOAC level) result quickly. Infrequent testing means reagents are not readily thawed and ready to go, standards need to be run each time and the laboratory must be well resourced to have trained scientists available."

Valente M et al.; Intern Med J. 2020 Jan;50(1):110-113. doi: 10.1111/imj.14652.

	dabigatran etexilate (PRADAXA®)	rivaroxaban (XARELTO®)	apixaban (ELIQUIS®)	edoxaban (LIXIANA®)
Target	Thrombin	Factor Xa	Factor Xa	Factor Xa
Bioavailability (%)	3-7% Not affected by food	- 80 to 100% for the 10 mg - 66% for the 15 and 20 mg (fasted)*	50% Not affected by food	62% Not affected by food
Prodrug	Yes – activated by esterase (CES1)	No	No	No
Half-life (hours)	11-13	5-13	8-15	10-14
T_{MAX} (hours)	0.5-2.0	2.0-4.0	3.0-4.0	1.0-2.0
Renal clearance	80%	33%	25%	50%
Metabolism	P-gp	P-gp CYP3A4	P-gp CYP3A4/5, 1A2, 2J2	P-gp CYP3A4/5

* these dose regimen have to be taken with food.

Fig. 1: Properties of non-vitamin K-dependent oral anticoagulants (adapted from Mega JL, Simon T. Lancet. 2015 Jul 18;386(9990):281-91.)

ClotPro® RVV-test and ECA-test show a high sensitivity for DOACs and a good agreement to lab based reference methods.

RVV-test

- Detection of direct factor-Xa (FXa) inhibitors
- Ref. No. 113012, 10 x 1 pc
- 30 days stability at room temperature
- 18 months stabilty at 2 - 8°C

ECA-test

- Detection of dabigatran
- Ref. No. 113013, 10 x 1 pc
- 30 days stability at room temperature
- 18 month stability at 2 - 8°C

ClotPro

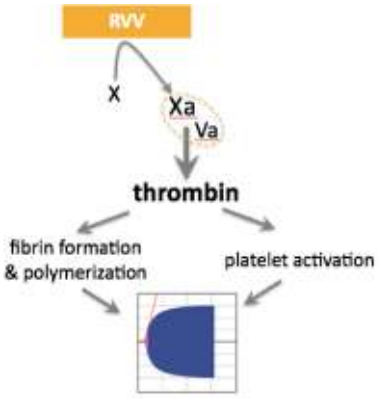
ClotPro® DOAC assays

Innovative tests for new therapeutics

RVV-test

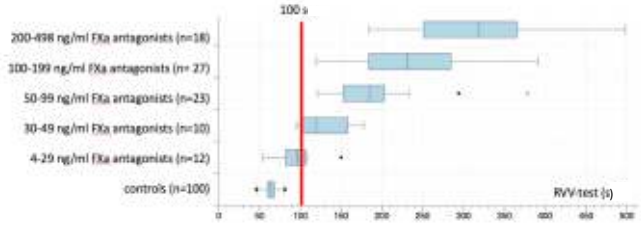
Detection of clotting via FXa – thrombin

Direct activation of FXa by the russel's viper snake venom (RVV)



Agreement vs. DOAC drug concentration

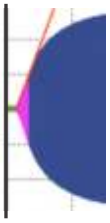
RVV-test clotting times



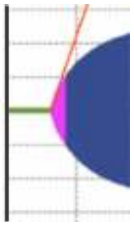
In a study 100 samples from individuals without anti-coagulant therapy had all **CTs < 100 s** in RVV-test (range: 46-81 s).

In a study including patients under FXa inhibitor treatment (edoxaban, rivaroxaban or apixaban, n=90) plasma concentrations of FXa inhibitors ≥50ng/ml (n = 68) were associated with **CTs ≥ 100 s** in RVV-test (range: 119-393 s).

No anticoagulant



FXa antagonist (rivaroxaban)



RVV-test CT is prolonged by

direct FXa antagonists

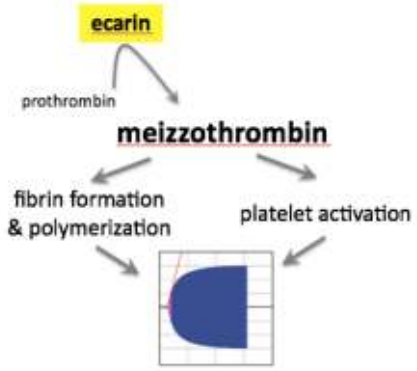
but also by…

- direct thrombin antagonists
- LMWH (from about 0.4 anti-Xa U/ml)
- UFH (high sensitivity)
- Vitamin K antagonists (2 vitamin K dependent factors)
- hemodilution / lack of fibrinogen (theoretical)

ECA-test

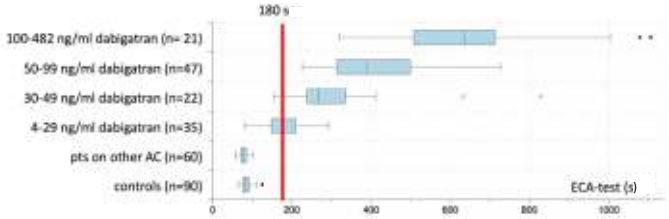
Detection of clotting via direct activation of prothrombin

Direct activation of prothrombin by the saw-scaled viper venom



Agreement vs. DOAC drug concentration

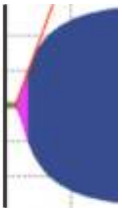
ECA-test clotting times



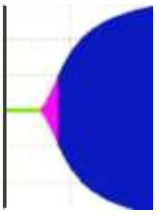
In a study 90 samples from individuals without anti-coagulant therapy all had **CTs < 180 s** in ECA-test (range: 65-125 s).

In a study including patients under dabigatran treatment (n=125), dabigatran plasma concentrations of ≥50 ng/ml (n=68) were associated with **CTs ≥ 180 s** in ECA-test (range: 226-1106 s).

No anticoagulant



thrombin antagonist (dabigatran)



ECA-test CT is prolonged by

direct thrombin antagonists

but also by…

- Vitamin K antagonists (theoretical)
- hemodilution / lack of fibrinogen (theoretical)

not affected by:

- LMWH / UFH
- direct FXa antagonists