RELATIONSHIP BETWEEN DABIGATRAN CONCENTRATIONS IN PLASMA AND RESULTS OF ROUTINE COAGULATION ASSAYS FOR PT, APTT, TT AND FIBRINOGEN

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BACKGRUOND Routine coagulation tests prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) and fibrinogen are affected by dabigatran therapy, but these assays are not standardized for assessment of its anticoagulant effect. However, exact knowledge of dabigatran impact on routine coagulation tests is a precondition for their correct interpretation.

AIM was to assess relationship between dabigatran concentrations and results of routine coagulation assays.

METHODS The study included 43 patients on dabigatran therapy. Plasma dabigatran concentrations were determined with DTI Innovance assay (Siemens, Germany) on BCSXP analyzer. All routine coagulation assays (PT, APTT, TT, fibrinogen) were also determined on BCSXP analyzer using commercial reagents (Table 1). The study was performed as an integral part of Croatian Science Foundation project HRZZ-IP-2016-06-8208.

RESULTS Dabigatran plasma concentrations ranged from **22 to 401 ng/mL (median 101 ng/mL; 95%CI 59-157 ng/mL).**

Table 1. Relationship between dabigatran concentrations and results of routine coagulation assays.

Assay	DABIG ng/mL	TT sec	PT % activity	PT INR	APTT sec	APTT ratio	Fibrinogen g/L
Commercial reagent (Siemens)	Innovance DTI	BC Thrombin	Innovin	Innovin	Actin FS	Actin FS	Multifibren U
N= 25, Median **95%CI** **IQR**	54 43 - 70 43 - 70	69 45-90 45-90	82 64 - 90 66 - 89	1.1 1.1 - 1.3 1.1 - 1.2	37.5 35 - 41 35 - 41	1.36 1.3 - 1.5 1.3 - 1.5	4.0 3.1 - 5.2 3.2 - 5.2
N=18, Median **95%CI** **IQR**	209 141 - 321 141 - 305	>150	50 44 - 55 44 - 54	1.5 1.3- 1.6 1.3 - 1.6	65.0 50 - 69 52 - 70	2.35 1.8 - 2.5 1.9 - 2.5	3.1 2.3 - 3.7 2.3 - 3.7
P	<0.0001	<0.0001	0.0003	0.0007	0.0001	0.0001	0.0208

IQR = interquartile range

TT was unmeasurable (>150s) in all patients with dabigatran levels above 100ng/ml with significantly higher (P<0.0001) dabigatran levels compared to patients with TT<150s (median 69s).

Among all patients, 16/43=0.37 had PT and 5/43=0.12 had APTT results in the reference range (PT>70%, APTT 23-32 sec, 0.8-1.2 ratio) while 27/43=0.63 and 38/43=0.88 had prolonged PT (<70%) and APTT (>32 sec; >1.2 ratio) respectively.

CONCLUSION The results of routine coagulation tests are strongly dependent on dabigatran plasma concentrations. Due to its high sensitivity, TT could be useful for detecting minimal dabigatran levels in plasma, but is too sensitive for dabigatran levels above 100 ng/mL. PT lacks sensitivity in detecting therapeutic levels of dabigatran but neither the APTT was invariably prolonged in patients with dabigatran levels below 100 ng/mL. In summary, routine coagulation tests PT, APTT and TT, although dependent on dabigatran concentrations, could not be used to assess therapeutic response to dabigatran therapy through a wide range of its plasma concentrations.

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