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A New Method for Determining Concentrations of Direct Oral Anticoagulants

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PB 1199 | A New Method for Determining Concentrations of Direct Oral Anticoagulants

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Background: Direct oral anticoagulants (DOACs) are commonly provided without monitoring. However, reliable assays to measure DOAC levels and activity in emergency situations are needed. We developed a test based on the inhibition of α_2 macroglobulin-thrombin (α_2 M-IIa)

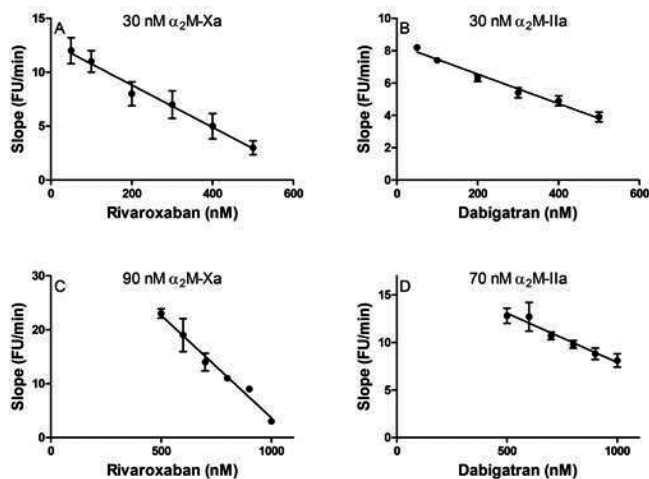


FIGURE 1 Dose-response of several DOAC concentrations at chosen α_2 M-Xa and α_2 M-IIa concentrations

TABLE 1 Correlation (Spearman) of rivaroxaban or dabigatran concentration (as determined by the new assay) with TG and other calibrated assays

Assay	Correlation coefficient	p-value	Assay	Correlation coefficient	p-value
Rivaroxaban			Dabigatran		
Calibrated prothrombin time (ng/ml)	0.468	0.002	Activated partial thromboplastin time (s)	0.581	0.002
Dilute Russel viper venom time (s)	0.760	0.000	Dilute Russel viper venom time (s)	0.649	0.001
Biophen DiXal (ng/ml)	0.915	0.000	Hemoclot thrombin inhibitor (ng/ml)	0.391	0.097
TG endogenous thrombin potential(nM.min)	-0.525	0.000	Ecarin chromogenic assay (ng/ml)	0.591	0.001
TG Peak (nM)	-0.550	0.000	TG endogenous thrombin potential(nM.min)	-0.323	0.100
TG lag time (min)	0.671	0.000	TG Peak (nM)	-0.354	0.201
TG time-to-peak (min)	0.702	0.000	TG lag time (min)	0.423	0.028
			TG time-to-peak (min)	0.339	0.084

by dabigatran (DAB) and of α_2 M-factor Xa (α_2 M-Xa) by rivaroxaban (RIV), making it possible to evaluate both DOAC classes in combination with thrombin generation (TG).

Aims: To quantify DOAC levels and activity in plasma.

Methods: Consenting patients using RIV (n=50) and DAB (n=28) were included. TG was performed in platelet poor plasma (5 pM tissue factor), with idarucizumab in calibrator wells for DAB samples. The new DOAC assays measured the effect of diluted plasma samples on Z-Gly-Gly-Arg-AMC conversion by α_2 M-Xa or α_2 M-IIa. The slopes of these curves were compared to a reference curve with known DOAC concentrations. DOAC levels were also estimated by 'classical' assays. Spearman correlation coefficients were determined.

Results: A concentration of 30 nM α_2 M-Xa or α_2 M-IIa was optimal to measure 50-500 nM RIV/DAB and 90 nM α_2 M-Xa or 70 nM α_2 M-IIa, respectively were optimal for 500-1000 nM RIV/DAB (Fig.1).

The intra- and inter-assay CV were below 2.5 % and 5% (n=2). Both the RIV and DAB assay correlated with TG parameters. The RIV assay correlated with 'classical' assays and had a very good correlation with Biophen DiXal. The DAB assay did not correlate with hemoclot thrombin inhibitor (probably since DAB concentrations were too low), but showed variable correlation with the other assays (Table1).

Conclusions: The new DOAC assays show good correlations with other assays that were confirmed to accurately assess DOAC levels (particularly the RIV assay with the Biophen DiXal, which had the best correlation with mass spectrometry). Our assay can simultaneously evaluate DOAC concentrations as well as the DOACs effect on thrombin generation, providing an overview of the anticoagulation status of a patient in relation to circulating DOAC levels.