# INTRODUCTION

FVIII and D-dimer are included in different prediction models to risk stratify for thrombotic recurrence or anticoagulation cessation. However, the optimal timing of their measurement related to the last drug dose is not sufficiently examined.

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# AIM

To determine FVIII and D-dimer levels at peak and trough plasma concentrations of direct oral anticoagulants (DOACs) in order to define optimal timing of blood drawing.

# METHOD

Concentrations of rivaroxaban (n=32), Apixaban (n=24) and dabigatran (n=28), D dimer levels and FVIII activities were measured at trough (before the next drug dose) and peak (two hours after drug intake) DOAC levels in circulation of outpatients during their regular control Clinical examination. Rivaroxaban and apixaban were determined using specific chromogenic anti-Fxa assay, dabigatran with Innovance DTI assay, FVIII with APTT based coagulometric method (Actin FS/FVIII deficient plasma) and D dimer by quantitative immunoturbidimetric assay using monoclonal antibody (Innovance D dimer), all from Siemens Healthineers, Germany on BCSXP analyzer. Statistical analysis was done with Wilcoxon and Friedman tests.

# FVIII and D-dimer values at trough and peak concentrations of direct oral anticoagulants: important considerations for using these tests in assissting clinical decision for risk stratification scheme

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### RESULTS

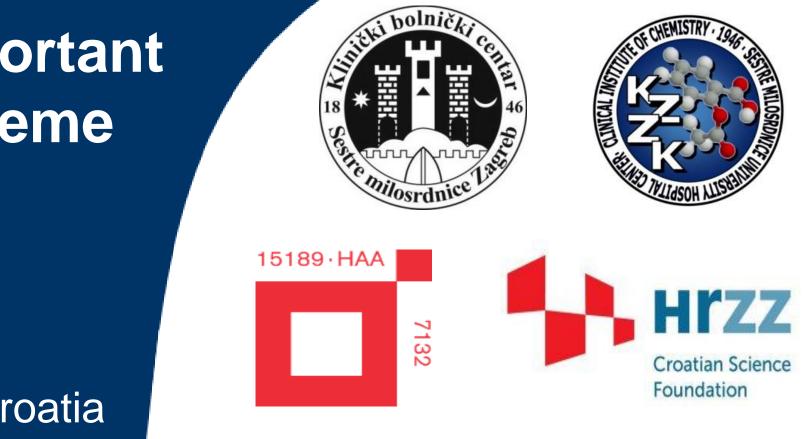
In contrast to D-dimer, FVIII values were significantly higher at trough in comparison with peak dabigatran and rivaroxaban concentrations (P = 0.013 and 0.024), whereas for apixaban FVIII also showed a trend of higher values at trough, but without significant difference (P=0.850, Table 1). Significantly higher values of both D-dimer and FVIII were measured at trough and peak drug levels of apixaban compared to dabigatran and rivaroxaban (Table 1, P\*).

	Peak drug	Trough drug	D-dimer (mg/L	D-dimer	FVIII (%) at	FVIII (%) at
DOAC	conc. ng/mL	conc. ng/mL	FEU) at peak	(mg/L FEU)	peak conc.	trough conc.
drug			conc.	at trough conc.		
	Median	Median	Median	Median	Median	Median
	(95%CI)	(95%CI)	(95%CI)	(95%CI)	(95%CI)	(95%CI)
	IQR	IQR	IQR	IQR	IQR	IQR
Dabigatran	125	39	0.23	0.22	70	100
N=28	(92-132)	(17-47)	(0.17-0.36)	(0.17-0.39)	(58-128)	(87-119)
	114-128	26-44	0.18-0.30	0.18-0.34	61-107	96-111
Ρ	0.001		0.563		0.013	
Rivaroxaba	238 (187-	21 (14-42)	0.22 (0.17-	0.29 (0.19-1.07)	122 (75-136)	159 (97-200)
n	360)	14-39	0.91)	0.20-0.82	83-131	115-191
N=32	201-337		0.17-0.64			
Ρ	0.001		0.203		0.024	
Apixaban	179	97	0.60	0.58	147	173
N=24	(148-213)	(94-107)	(0.35-1.51)	(0.40-1.69)	(124-201)	(105-196)
	140-208	98-111	0.30-1.50	0.39-1.60	120-201	101-201
Ρ	<0.001		0.909		0.850	
<b>P*</b>			0.008	0.001	0.026	0.001

95%CI = 95% confidence interval; IQR = interquartile range; P< 0.05 was considered statistically significant \*P values for trough and peak values of D-dimer and FVIII levels in patients treated with apixaban compared with dabigatran and rivaroxaban

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Table 1. Results of factor FVIII (FVIII) and D-dimer levels at peak and trough concentrations of DOACs.



# CONCLUSIONS

**Plasma concentration** of DOACs significantly affects FVIII values, unlike Ddimer. These findings are important when using these tests in assissting clinical decisions related to risk stratification schemes for recurrent thrombotic event or anticoagulation cessation. For FVIII measurement blood drawing should be performed at trough **DOAC levels** exclusively, whereas **D-dimer may be** measured at both trough or peak drug levels in circulation.

# **CONTACT INFORMATION**

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