Stato sulla discussione sulle indicazioni alla misurazione dei DOAC

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ON MY MIND

Urgent Need to Measure Effects of Direct Oral Anticoagulants

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The direct oral anticoagulants (DOACs), which include dabigatran, rivaroxaban, apixaban, and edoxaban, were designed to be given in fixed doses without routine coagulation monitoring. When administered in this manner in trials that included >71 000 patients with atrial fibrillation] and >27000 patients with venous thromboem

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Although routine coagulation monitoring is unnecessary, there is an urgent need for readily and rapidly available tests to measure the DOACs. This need will increase with the introduction of costly reversal agents such as idarucizumab for dabigatran[3] and andexanet alfa for rivaroxaban, apixaban, and edoxaban.[4] Idarucizumab

Although currently available global tests of coagulation such as the activated partial thromboplastin time (aPTT) and prothrombin time (PT) can be useful to assess the anticoagulant effects of dabigatran and some of the oral factor Xa inhibitors, respectively, the sensitivity of these tests is variable and reagent dependent.[5] Regardless of reagent, the PT is less responsive to apixaban and

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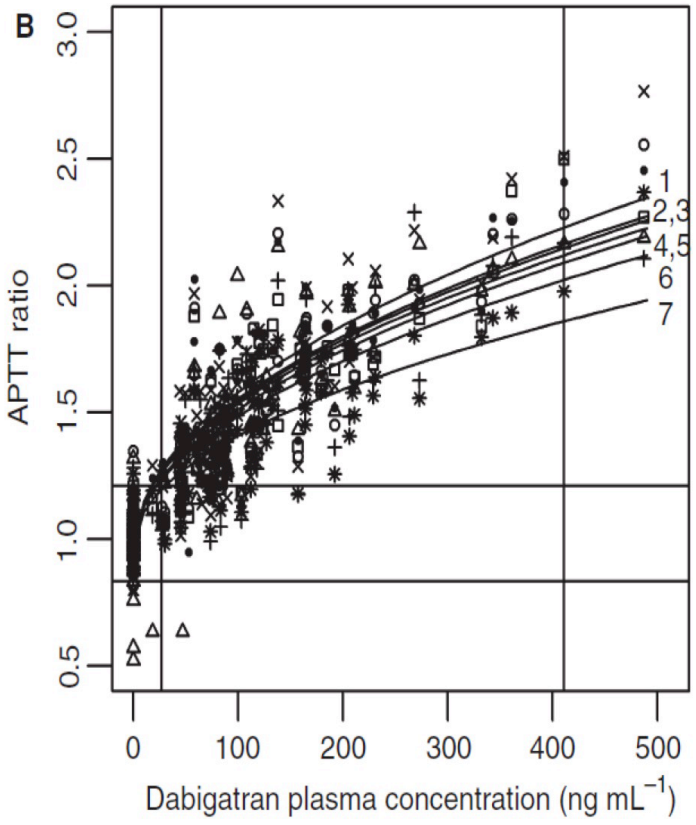
APTT commerciali & Dabigatran



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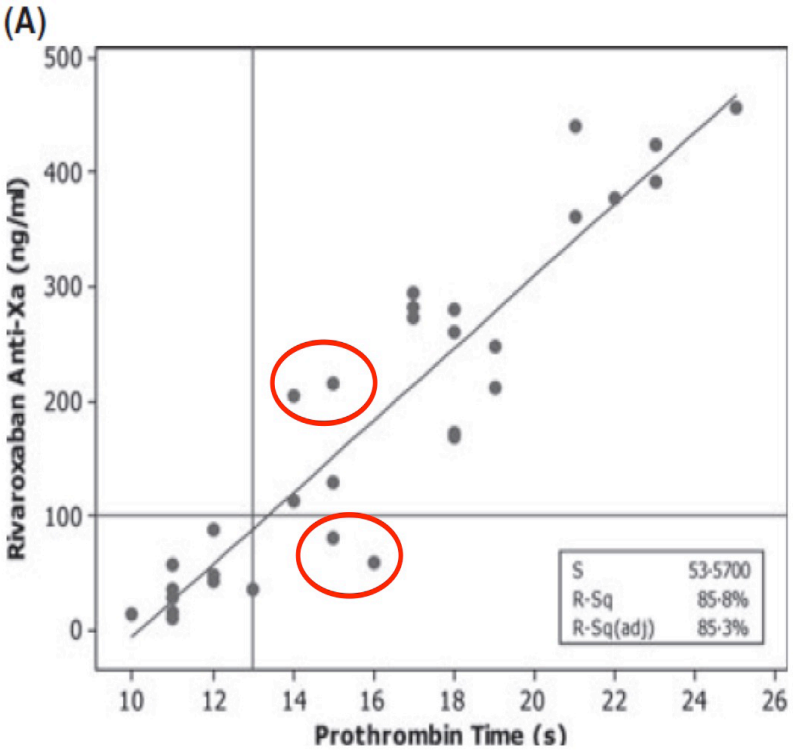
Hawes EM et al, 2013

Rivaroxaban & PT



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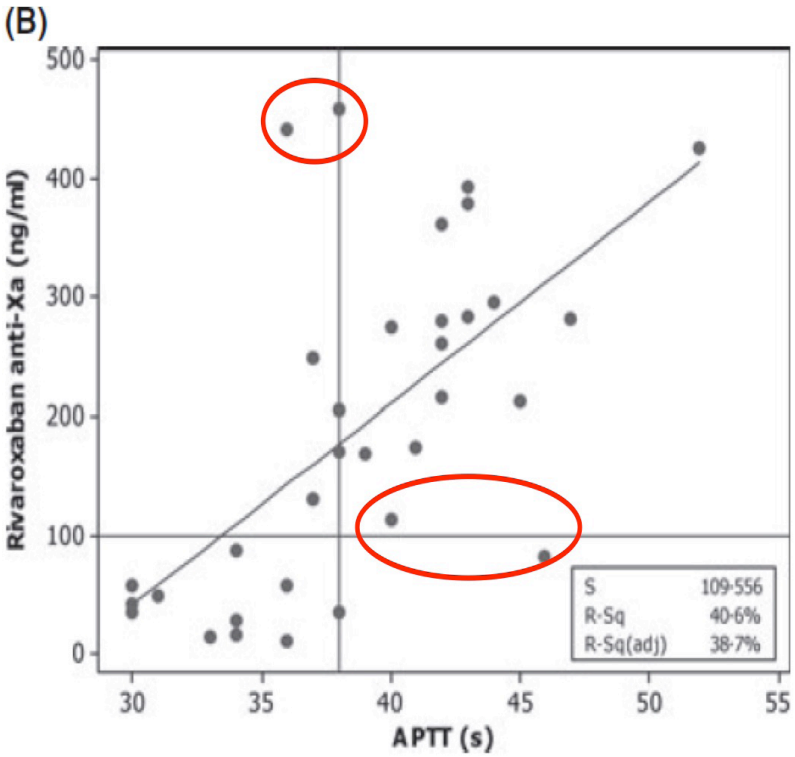
Rodgers R et al, 2013

Rivaroxaban & APTT



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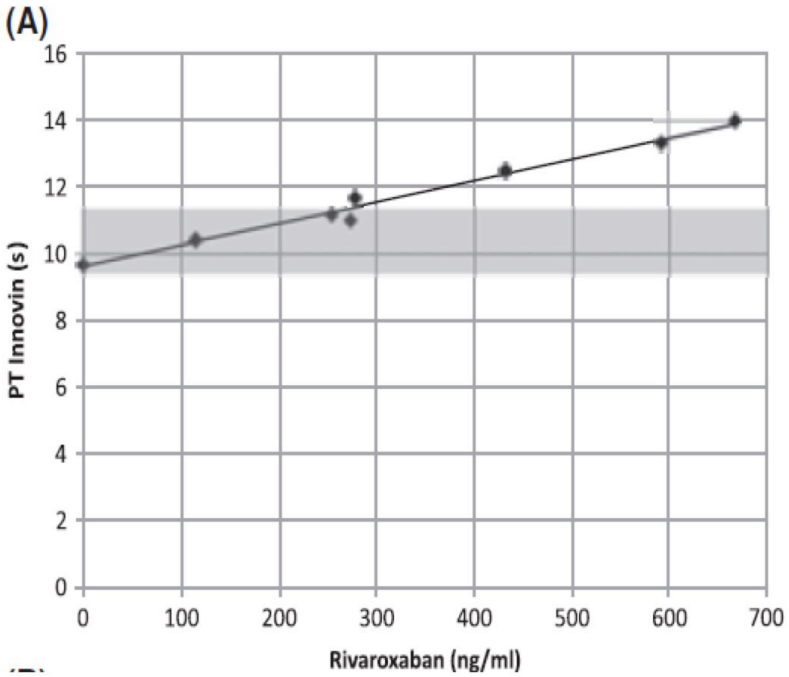
Rodgers R et al, 2013

Rivaroxaban & PT



Van Veen JJ et al, 2012

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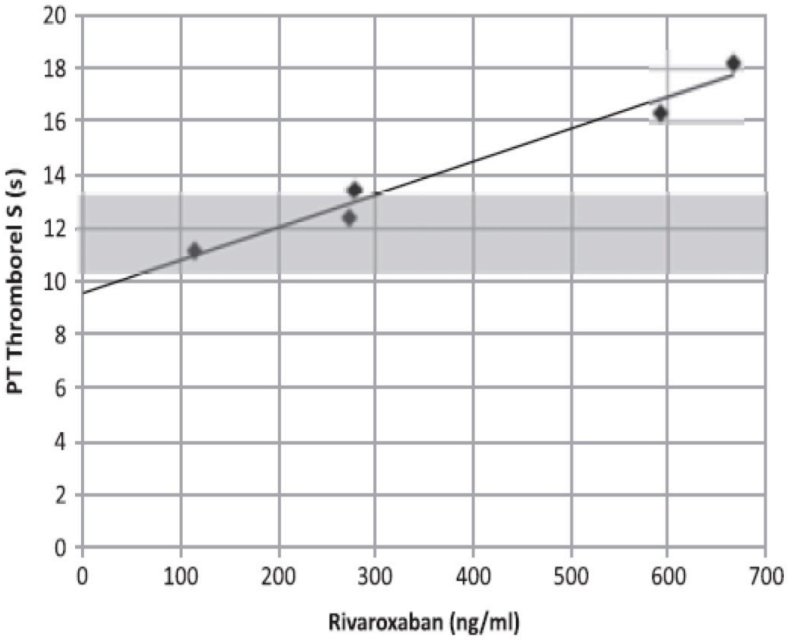
Rivaroxaban & PT



Van Veen JJ et al, 2012

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Rivaroxaban & PT/APTT

Table I. Comparison of rivaroxaban concentration and effect on PT and APTT.

	<125 ng/ml	<223 ng/ml	>223 ng/ml
Normal PT	65/67 (97%)	79/88 (90%)	10/37 (27%)
Normal APTT	61/66 (92%)	73/87 (84%)	10/37 (27%)
Normal PT & APTT	58/65 (89%)	68/86 (79%)	6/37 (16%)
Raised PT, normal APTT	2/65 (3%)	5/86 (6%)	4/37 (11%)
Normal PT, raised APTT	5/65 (8%)	9/86 (10%)	4/37 (11%)
Raised PT & APTT	0/65 (0%)	4/86 (5%)	23/37 (62%)
Increase in PT*	3/32 (9%)	10/41 (24%)	19/20 (95%)

Platton S et al, 2016

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drug. Therefore, more accurate tests are needed. Such tests are currently available in research facilities and include the diluted thrombin time and ecarin clot time or ecarin chromogenic assay for dabigatran, as well as chromogenic anti–factor Xa assays for rivaroxaban, apixaban, and edoxaban.[5] Unfortunately, these tests are not widely available, and even if available, the turnaround time is often too slow to be useful. This needs to change.

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Why is the need for these tests so urgent? Quantification of plasma concentrations of the DOACs is critical when assessing their potential contribution to serious bleeding, when making decisions about the timing of urgent surgery or interventions, or when determining whether patients with acute ischemic stroke can safely be given fibrinolytic therapy. Patients with elevated drug levels in these settings may benefit from the administration of a reversal agent, whereas those with little or no circulating drug will not. In urgent situations, clinicians may adminis-

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Can we achieve this goal? All modern coagulometers are capable of performing chromogenic assays with a turnaround time similar to that for the aPTT or PT, and anti–factor Xa assays are already available for quantifying levels of heparin or low-molecular-weight heparin. Commercial anti–factor Xa assays for rivaroxaban and apixaban and a diluted thrombin time and ecarin chromogenic assay for dabigatran are available, and an anti–factor Xa assay for edoxaban soon will be (Table). Adoption of these assays into practice requires their regulatory approval for clinical use and their widespread introduction into busy emergency departments. We urge regulatory agencies and hospitals to get on board to make this happen.

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VEQ FCSA per DOAC

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VEQ FCSA DOAC 2017
Plasmi

- B (no DOAC)
- D (DABI bassa conc.)
- C (RIVA media conc.)
- E (API media conc.)

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VEQ FCSA DOAC
Invio

- Sono stati fatti 275 invii
- Abbiamo ricevuto risposte
- 237 per PT, APTT
- 88 per TT
- 76 per conc. DABI
- 65 per conc. RIVA
- 58 per conc. API

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VEQ FCSA DOAC
Metodi

- E' stata chiesta la misura di
- PT
- APTT
- Tempo di trombina (TT)
- Concentrazione di DABI, RIVA, API (ng/mL)

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VEQ FCSA Dabigatran
Risultati

Test	Plasmi	
	B (no DABI)	D (DABI, 43 ng/mL)

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VEQ FCSA Dabigatran
Risultati

Test	Plasmi	
	B (no DABI)	D (DABI, 43 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.06 (CV = 3.8%)

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VEQ FCSA Dabigatran
Risultati

Test	Plasmi	
	B (no DABI)	D (DABI, 43 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.06 (CV = 3.8%)
APTT ratio	1.00 (CV = 6.2%)	1.32 (CV = 7.1%)

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VEQ FCSA Dabigatran
Risultati

Test	Plasmi	
	B (no DABI)	D (DABI, 43 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.06 (CV = 3.8%)
APTT ratio	1.00 (CV = 6.2%)	1.32 (CV = 7.1%)
TT ratio	1.00 (CV = 12.3%)	7.3 (CV = 43.3%)

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VEQ FCSA Dabigatran
Risultati

Test	Plasmi	
	B (no DABI)	D (DABI, 43 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.06 (CV = 3.8%)
APTT ratio	1.00 (CV = 6.2%)	1.32 (CV = 7.1%)
TT ratio	1.00 (CV = 12.3%)	7.3 (CV = 43.3%)
Dabigatran (ng/mL)	<30 ng/mL (96% dei Lab)	43 ng/mL (CV = 39%)

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VEQ FCSA Rivaroxaban
Risultati

Test	Plasmi	
	B (no RIVA)	C (RIVA, 315 ng/mL)

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VEQ FCSA Rivaroxaban
Risultati

Test	Plasmi	
	B (no RIVA)	C (RIVA, 315 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.70 (CV = 15.2%)

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VEQ FCSA Rivaroxaban
Risultati

Test	Plasmi	
	B (no RIVA)	C (RIVA, 315 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.70 (CV = 15.2%)
APTT ratio	1.00 (CV = 6.2%)	1.45 (CV = 10.8%)

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VEQ FCSA Rivaroxaban
Risultati

Test	Plasmi	
	B (no RIVA)	C (RIVA, 315 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.70 (CV = 15.2%)
APTT ratio	1.00 (CV = 6.2%)	1.45 (CV = 10.8%)
TT ratio	1.00 (CV = 12.3%)	1.03 (CV = 8.8%)

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VEQ FCSA Rivaroxaban
Risultati

Test	Plasmi	
	B (no RIVA)	C (RIVA, 315 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.70 (CV = 15.2%)
APTT ratio	1.00 (CV = 6.2%)	1.45 (CV = 10.8%)
TT ratio	1.00 (CV = 12.3%)	1.03 (CV = 8.8%)
Rivaroxaban (ng/mL)	<30 ng/mL (98% dei lab)	315 ng/mL (CV = 17%)

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VEQ FCSA Apixaban
Risultati

Test	Plasmi	
	B (no API)	E (API, 285 ng/mL)

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VEQ FCSA Apixaban
Risultati

Test	Plasmi	
	B (no API)	E (API, 285 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.29 (CV = 9.6%)

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VEQ FCSA Apixaban
Risultati

Test	Plasmi	
	B (no API)	E (API, 285 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.29 (CV = 9.6%)
APTT ratio	1.00 (CV = 6.2%)	1.19 (CV = 8.2%)

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VEQ FCSA Apixaban
Risultati

Test	Plasmi	
	B (no API)	E (API, 285 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.29 (CV = 9.6%)
APTT ratio	1.00 (CV = 6.2%)	1.19 (CV = 8.2%)
TT ratio	1.00 (CV = 12.3%)	1.00 (CV = 8.0%)

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VEQ FCSA Apixaban
Risultati

Test	Plasmi	
	B (no API)	E (API, 285 ng/mL)
PT ratio	1.03 (CV = 3.5%)	1.29 (CV = 9.6%)
APTT ratio	1.00 (CV = 6.2%)	1.19 (CV = 8.2%)
TT ratio	1.00 (CV = 12.3%)	1.00 (CV = 8.0%)
Apixaban (ng/mL)	<30 ng/mL (98% dei Lab)	285 ng/mL (CV = 26%)

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VEQ FCSA DOAC
Conclusioni

- PT
- Insensibile per DABI (bassa conc.) e per API (media conc.)
- Sensibile per RIVA (media conc.)
- APTT
- Sensibile per DABI e RIVA, insensibile per API
- TT
- Altamente sensibile anche a basse conc. per DABI,
- Insensibile per RIVA e API

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