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Heparin Calibrated Anti-Xa Assays for the Measurement of Low Levels of Direct Factor Xa Inhibitors

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PB 2151 | Heparin Calibrated Anti-Xa Assays for the Measurement of Low Levels of Direct Factor Xa Inhibitors

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Background: Apixaban, edoxaban and rivaroxaban do not require frequent monitoring but an assessment of the intensity of anticoagulation may be required in emergent or elective surgery. Some experts reported that anti-Xa activity below 0.1 IU/mL using heparin calibrated chromogenic assays may assert the absence of clinically relevant (i.e. < 30 or < 50 ng/mL depending on the clinical situation) direct factor Xa levels. However, it is not clear if difference in response will depend on the anti-Xa agent and also on the chromogenic anti-Xa kit used to assess the anti-Xa activity.

Aims: To assess if a cut-off of 0.1 UI anti-Xa/mL is able to exclude apixaban, rivaroxaban or edoxaban concentration < 30 ng/mL or < 50 ng/mL using different heparin calibrated chromogenic anti-Xa kits.

Methods: Apixaban, edoxaban and rivaroxaban were added to normal pooled plasma at increasing concentrations ranging from 0 to 500 ng/mL. Anti-Xa activities were measured using

- (1) STA®-Liquid Anti-Xa (STA®LAX) on a STA-R Evolution Coagulometer,
- (2) Biophen®Heparin LRT (BP®LRT) on a STA-R Evolution coagulometer and
- (3) HemosIL®-Liquid Anti-Xa (IL®LAX) on a ACL-TOP 700 according to manufacturer recommendations.

Results: At 30 ng/mL of rivaroxaban, BP®LRT, STA®LAX and IL®LAX provided anti-Xa results >0.1 IU/mL. At 30 ng/mL of apixaban or edoxaban, BP®LRT and IL®LAX were below the cut-off but the STA®LAX was not. At a concentration of 50 ng/mL, only edoxaban with the BP®LRT kit showed an anti-Xa activity < 0.1 UI/mL.

Conclusions: Low (< 0.1 IU/mL) anti-Xa activity is not safe to exclude clinically relevant direct factor Xa levels and should be avoided. It can only inform if the drug is present or not. Chromogenic anti-Xa assays calibrated against the appropriate agent and using the appropriate

TABLE 1 Anti-Xa activities using STA®LAX on a STA-R Evolution Coagulometer, BP®LRT on a STA-R Evolution coagulometer and (3) IL®LAX on a ACL-TOP 700

concentration (ng/mL)	anticoagulant	STA®LAX (UI/mL)	BP®LRT (UI/mL)	IL®LAX (UI/mL)
30	Rivaroxaban	0,19	0,12	0,08
30	Apixaban	0,09	0,03	0,04
30	Endoxaban	0,07	0,02	0,02
50	Rivaroxaban	0,45	0,34	0,16
50	Apixaban	0,17	0,10	0,07
50	Endoxaban	0,13	0,06	0,04

procedure remains the more accurate method to assess accurately low levels of direct FXa inhibitors.

PB 2152 | Efficacy of a Novel Contact Pathway Inhibitor, Ir-CPI, on in vitro Clotting Induced by PCI Catheter Segment

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Background: Ir-CPI, a protein derived from the tick *Ixodes ricinus* salivary, is a serine protease inhibitor of both factor XIa (FXIa) and FXIIa. In patients undergoing percutaneous coronary intervention (PCI), catheter thrombosis may occur as catheters trigger activation of FXII/FXI.

Aims: The aim of this study was to evaluate the effect of Ir-CPI on in vitro clotting induced by PCI catheter segment.

Methods: Catheter segments were pressed flat, shaped into rings and placed around the perimeter of wells (96-well plate), leaving the center of the well unobstructed. To the wells were added serial dilution of Ir-CPI (until 10 µM) with normal pooled plasma (NPP) or plasmas deficient in FXI or FXII. After incubation at 37°C and addition of a CaCl₂ solution, clot formation was assessed by monitoring absorbance at 340nm. Time to reach one-half maximal absorbance (IC50) was defined as the clotting time. Thrombin generation test (TGT) was also assessed using catheter segment as trigger of the process. Positive inhibitory controls were used (fondaparinux, enoxaparin).

Results: Presence of the catheter reduced the clotting time of NPP; an effect reversed by the addition of Ir-CPI. At high concentrations (> 5µM), Ir-CPI allowed to overpass the clotting time without catheter. On TGT (Fig 1), catheter segments decreased lag time and time

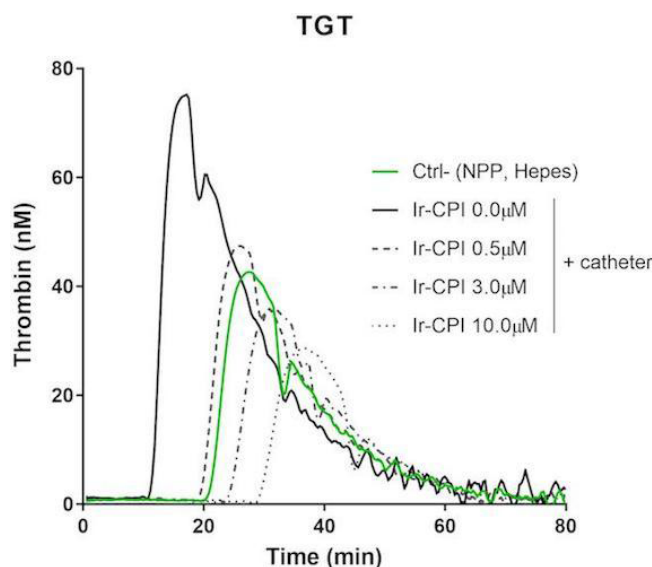


FIGURE 1 Effect of Ir-CPI on Thrombin Generation Time (TGT) in NPP exposed to PCI catheter segments