Evaluating global coagulation assays in patients with venous thromboembolism

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RESEARCH WEEK
5-9 OCTOBER 2020
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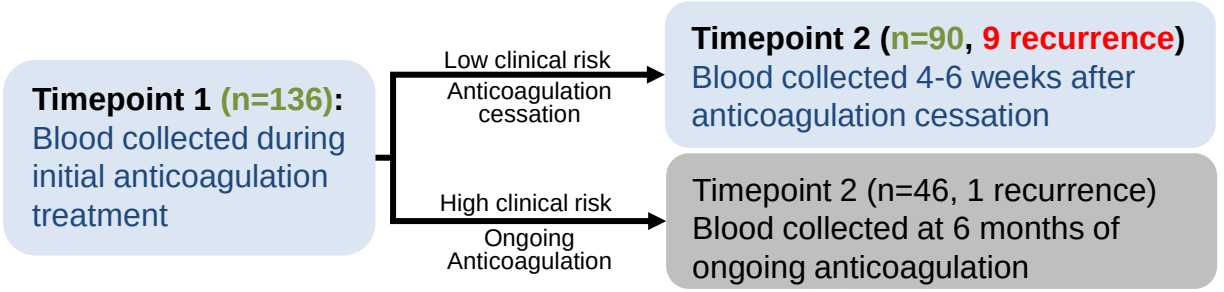
Background and methods

- **Venous thromboembolism (VTE)**, including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a prevalent disease worldwide associated with high recurrence, significant morbidity and mortality[1].
- Current routine coagulation tests cannot reliably predict recurrence, although abnormal D-dimer level is associated with high risk of recurrence[2].
- **Global coagulation assays (GCA)** may provide a holistic evaluation of total clot formation and lysis[3] and we hypothesise that they may have utility in risk stratification of VTE recurrence in clinical setting. Such assays include:
  - **Calibrated automated thrombogram (CAT)** – evaluates thrombin generation
  - **Overall haemostatic potential (OHP)** assay – evaluates fibrin generation

1. Naess IA et al. Journal of thrombosis and haemostasis. 2007;5(4):692-9.
2. Palareti G et al. The New England journal of medicine. 2006;355(17):1780-9
3. Lim HY et al. Thrombosis research. 2019;179:45-55.

- VTE patients and healthy normal controls were recruited at the Northern Hospital.
- For normal controls, blood was collected once only.
- For VTE patients, blood was collected at two different timepoints described in the diagram below.
- Baseline blood tests were performed. CAT and OHP were performed on platelet-poor plasma, obtained by double centrifugation.
- Patients were followed up for a median of 19 months.
- The focus of this poster presentation is the patient subgroup who have ceased anticoagulation after initial treatment.



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Results and discussion

OHP of subjects and controls at Timepoint 1 and 2

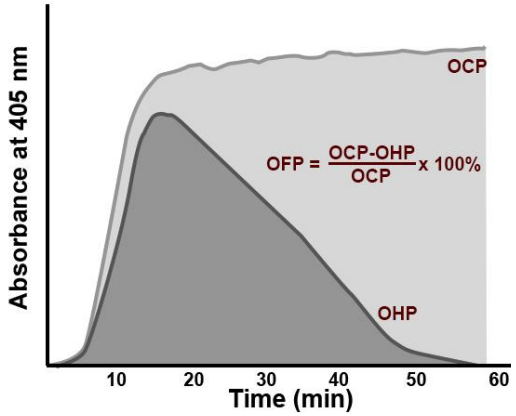

Figure 1. Standard OHP assay curve.

OCP: overall coagulation potential – amount of fibrin generated, reported as area under OCP curve

OHP: overall haemostatic potential – balance of fibrin generation and lysis, reported as area under OHP curve

OFP: overall coagulation potential – amount of fibrin lysed, reported as a percentage difference between OCP and OHP

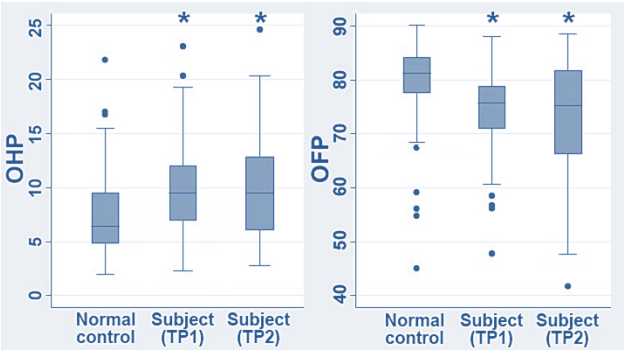

Figure 2. OHP at Timepoint 1 and 2 (TP1 & TP2).

- **Elevated OHP** and **reduced OFP** at both TP1 and TP2 when compared to control (9.5 and 9.6 vs 6.4, 75.5% and 74.8% vs 81.2%, respectively).
- Results indicate there is persistently elevated thrombin generation and hypofibrinolysis in VTE subjects compared to normal controls.

*** Multivariate analysis (age and gender adjusted) compared to normal controls, p < 0.05**

CAT of subjects and controls at Timepoint 2

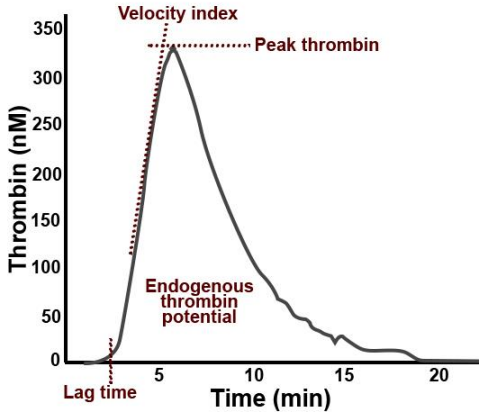

Figure 3. Standard CAT assay curve.

Lag time: time until thrombin generation

Endogenous thrombin potential (ETP): amount of thrombin generated, area under the curve

Peak thrombin: maximum concentration of thrombin

Velocity index: maximum rate of thrombin generation

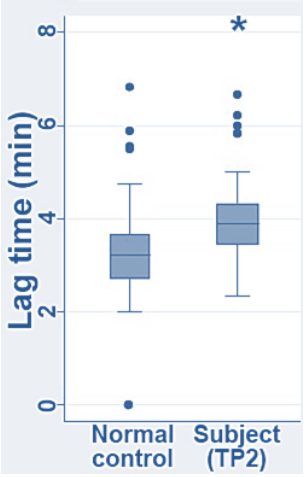

Figure 4. CAT at Timepoint 2 (TP2) after anticoagulation cessation compared to normal controls.

- **Shortened lag time** at TP2 compared to controls (3.9 min vs 5.9 min), suggesting a more rapid thrombin generation.
- No significant difference in ETP, peak thrombin and velocity index when compared to controls.

*** Multivariate analysis (age and gender adjusted) compared to normal controls, p < 0.05**

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Results and discussion (cont.), Conclusion

GCA of patients with and without VTE recurrence

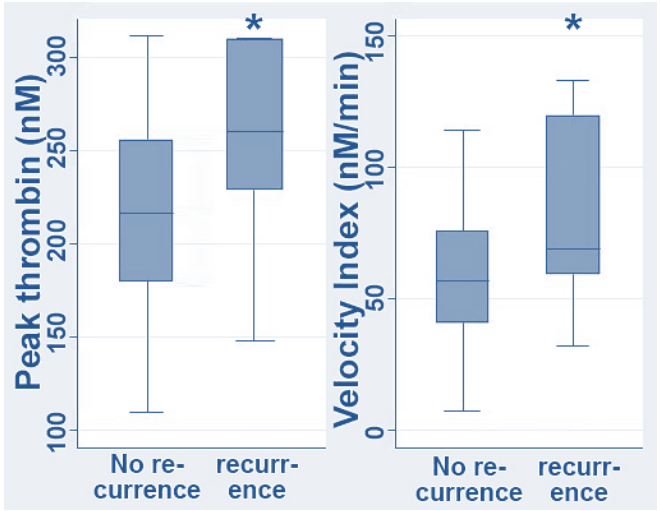

Figure 5. Peak thrombin and velocity index at Timepoint 2 (TP2) for patients with and without VTE recurrence

- **Higher peak thrombin** (259 vs 212 nM) and **velocity index** (83.9 vs 59.5 nM/min) at TP2 (anticoagulation ceased) in those who developed VTE recurrence, compared to those that did not.
- No significant difference in OHP assay between the two groups.

*** Univariate analysis compared to no recurrence group, $p < 0.05$**

Conclusions

- Patients who later developed recurrent VTE displayed significantly higher peak thrombin and velocity index 4-6 weeks after cessation of anticoagulation, compared to those who did not develop recurrent VTE.
- Compared to normal controls, VTE patients display increased thrombin generation and reduced fibrinolysis as demonstrated by CAT and OHP.

Acknowledgment

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