A novel rapid fibrinogen assay based on thrombin generation and turbidity

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INTRODUCTION

- A rapid point-of-care test to measure fibrinogen levels is crucial to adequately treat patients with major blood loss.
- Obtaining fibrinogen test results, such as the Clauss assay or alternatives, are often costly and too time consuming in emergency situations.
- Here, we used a mathematical model using on thrombin generation- and turbidity curves as inputs derive the fibrinogen levels in patient samples.

AIM

To compare the predicted fibrinogen levels from our mathematical model to measured fibrinogen levels (Clauss assay) in diagnostically challenging patients

METHODS

- Collected 44 citrated plasma samples
  - Fibrinogen levels: 1.1 – 16.6 g/L
  - Part of the samples contain anticoagulants (table 1)
  - Retrospectively collected the prothrombin time, D-dimer levels, anti-Xa levels and the INR if available
- Turbidity- and the thrombin generation curves were measured simultaneously and used as input for the model to predict the fibrinogen level of the sample.
- Fibrinogen levels were measured with the Clauss assay (observed fibrinogen levels).
- Comparison between predicted and observed fibrinogen levels using a correlation.

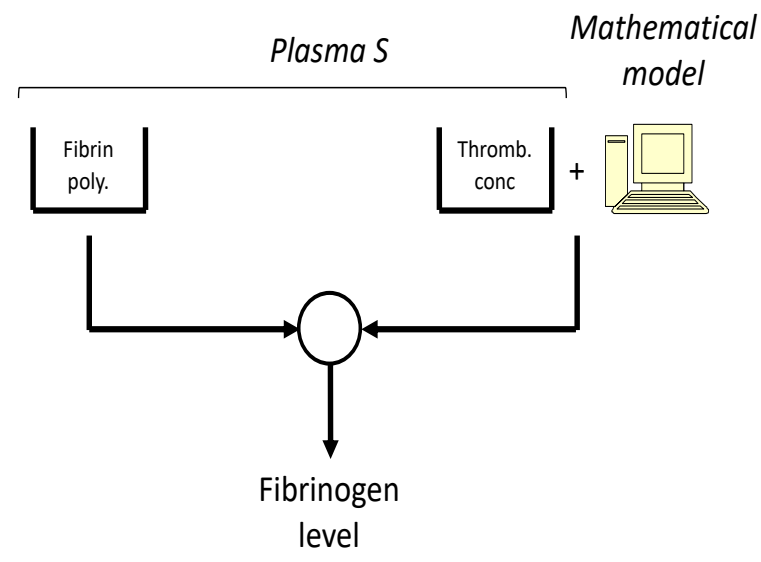

Figure 1. Schematic overview of the model which uses fibrin polymerization (turbidity curves) and the activated thrombin concentration (thrombin generation curve) to predict the fibrin level in plasma.

CONCLUSION

- **Our method can determine the fibrinogen concentration very well.**
- **Fibrinogen levels in plasma samples with strongly abnormal thrombin generation or clotting curves (e.g., due to high levels of anticoagulants) could not be determined.**

WORK IN PROGRESS

- Further training of the model with additional measurements will improve the accuracy and speed of the fibrinogen concentration determination
- Change the assay (e.g. with Heparinase) to obtain normal clotting curves in a wider range of patients
- Further develop the model into a complete point-of-care test for on-site application in the clinic.

RESULTS

Patient characteristics

Table 1. Patient sample characteristics

Characteristic	Measured in number of patients	(%)	Median	[IQR]
Prothrombin time	44	(100%)	13.6	[11.7 - 17.9]
D-dimer	18	(41%)	2.8	[0.8 - 4.8]
Anti-Xa	14	(32%)	0.16	[0.08 - 0.21]
INR	26	(59%)	1.3	[1.0 – 2.3]
Observed fibrinogen levels (Clauss)	44	(100%)	4.4	[3.3 - 6.3]
Predicted fibrinogen levels (Mathematical model)	36	(82%)	4.2	[3.2 - 6.0]
Anticoagulant medication				
Heparin	22	(50%)		
Vitamin K antagonist	5	(11%)		
Aspirin	2	(5%)		
DOAC	2	(5%)		

Performance predicted fibrinogen levels

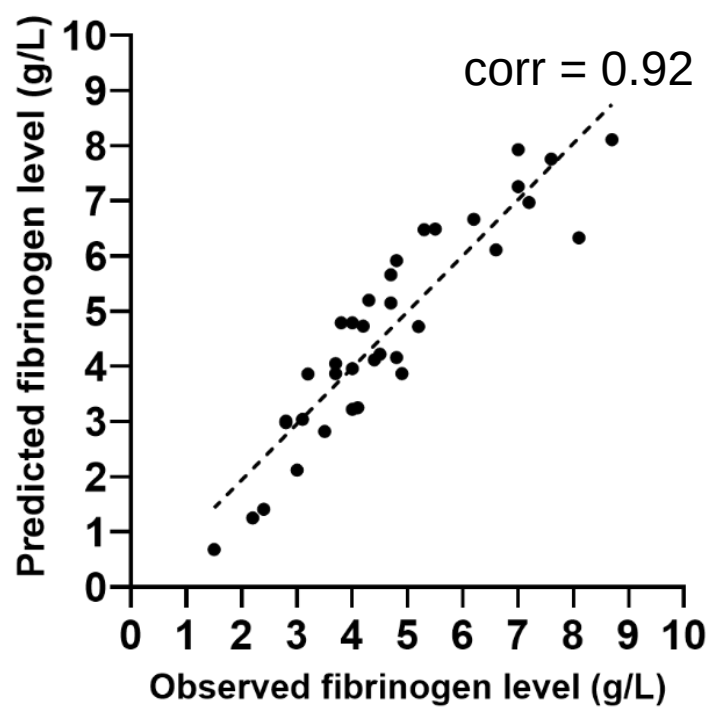

Figure 2. Plotted correlation between the predicted- the observed fibrinogen levels, measured with the Clauss assay.

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