# Coagulation status of critically ill patients with liver disease assessed using a novel thrombin generation analyser


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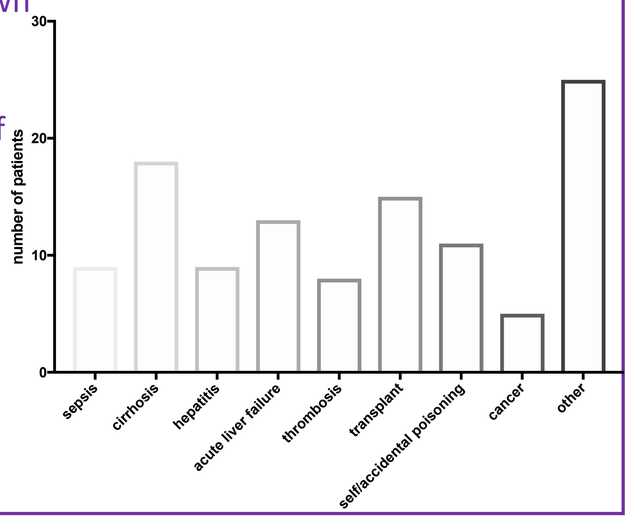
**INTRODUCTION:** The liver synthesises the majority of pro- and anti-coagulant and fibrinolytic proteins. Complex alterations in the haemostatic system occur in patients with advanced liver disease, which may result in life threatening thrombosis and bleeding. Current haemostatic tests, such as the prothrombin time (PT), represent only 5 % of thrombin generation and do not assess the effects of natural anti-coagulants. Therefore they have limited predictive value for bleeding.

## Study Group

Patient samples were obtained from the Intensive Care Study of Coagulopathy-2 (ISOC-2) trial. ISOC-2 was a cross-sectional study of patients admitted to critical care who had abnormal clotting. This was defined as a prolonged PT, greater than 3 seconds above the upper limit of the normal range. Samples were taken as shown in methods. 101 patients recruited had liver disease of varying degrees.




## AIM

**Is thrombin generation (TG) a better haemostatic test for predicting bleeding in critically ill patients with liver disease?**

## Methods

PPP samples were thawed for 10 min at 37 °C (*n*= 101). There were four time points used in the study; initial sample, before plasma, after plasma and end of study (5 days). Only a small number of patients received plasma (*n*= 32). TG was performed using a novel analyser manufactured by Stago, ST Genesia, and STG-thromboscreen ± thrombomodulin (TM) (intermediate tissue factor concentration).

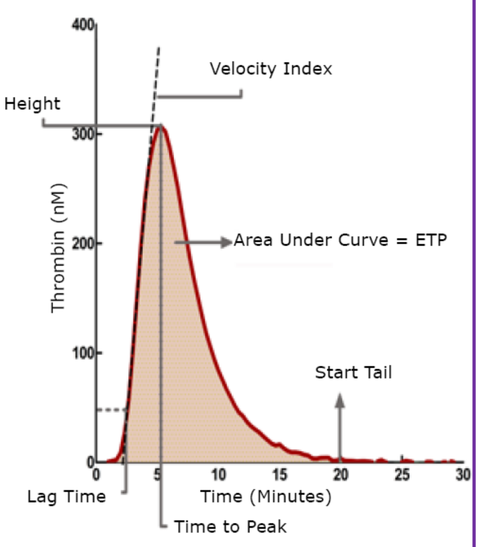
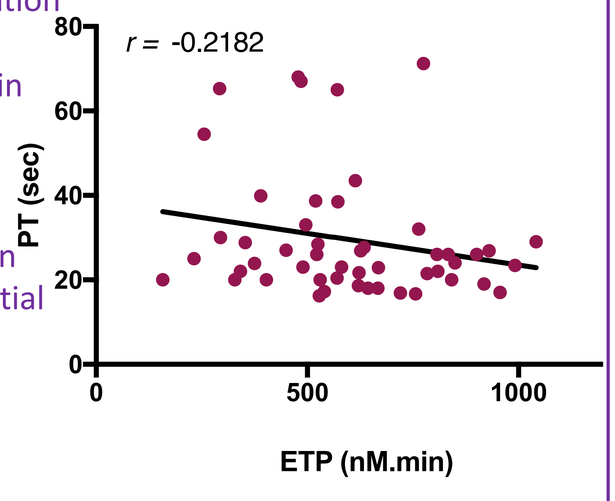



**Figure 1: There is no correlation between the patients endogenous thrombin potential and PT**

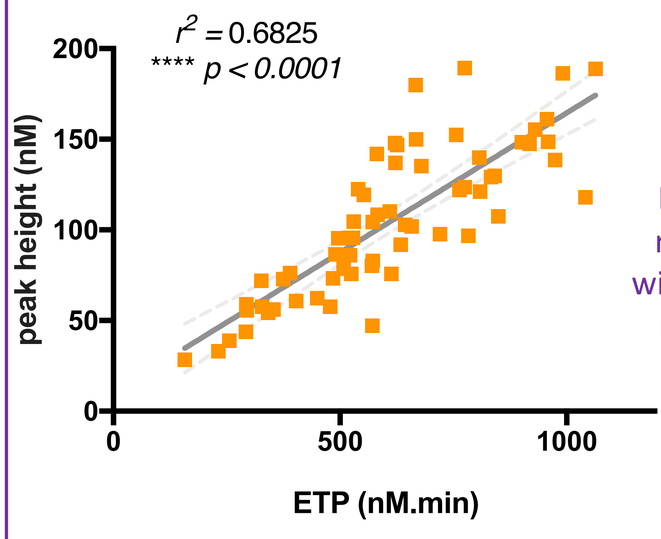
There was no correlation between the endogenous thrombin potential (ETP) and PT. Additionally there was no relationship between TG and activated partial thromboplastin time (APTT), Clauss fibrinogen or platelet count (not shown).




## Conclusion

**Measurement of TG and addition of TM provides a global assessment of pro- and anti- coagulant factors, indicating that haemostasis is balanced in critically ill patients with liver disease. The ST Genesia may be used clinically to identify patients who do not require plasma transfusion**

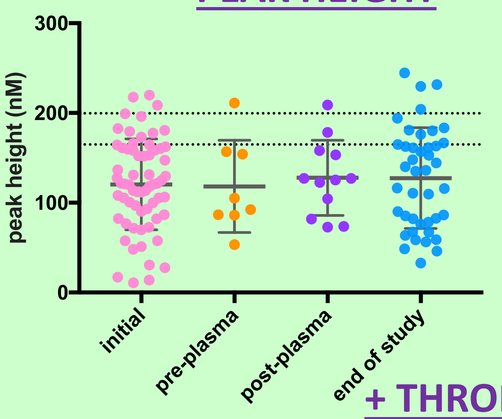
**Figure 3: Peak height as a predictor of ETP**



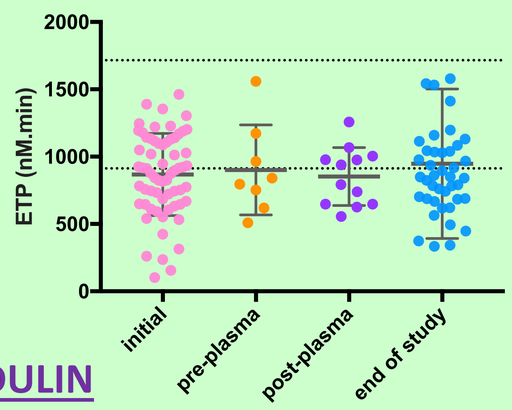

There was a strong positive correlation between peak height and ETP. Peak height was rapidly obtained within 5.52 ± 1.49 min and may be used to predict ETP when monitoring critically ill patients.

**Figure 2: Addition of thrombomodulin provides more accurate assessment of coagulation potential than conventional lab tests**

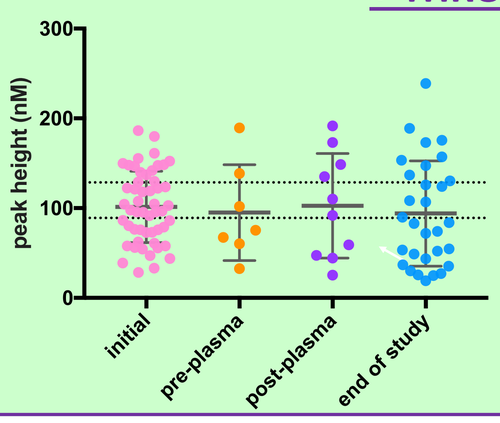
### PEAK HEIGHT

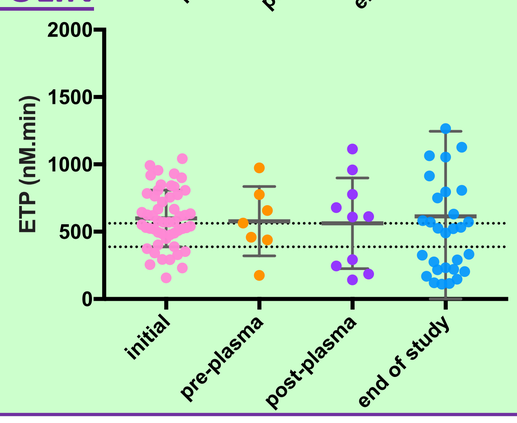



### ETP




### + THROMBOMODULIN

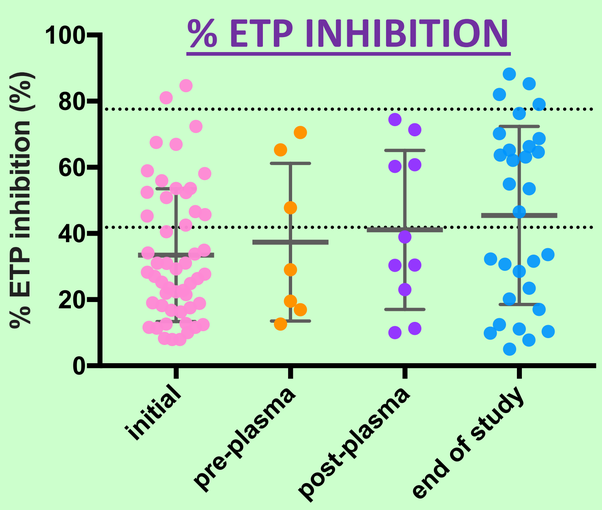



Despite a prolonged PT, 50 % of patients had normal ETP (912.4 – 1715.6 nM.min). The remaining 50 % were below the normal limit (< 912.4 nM.min).

After addition of TM only 20 % of patients had reduced ETP. The remaining patients were found to have normal or elevated TG ability; 38 and 42 % respectively.

### % ETP INHIBITION




Addition of TM reduced TG and was recorded as percentage ETP inhibition, which was lower in patients (33.46 ± 20.06 %) than in healthy volunteers (59.5 ± 17.86 %).


**Acknowledgements:** The ST Genesia and reagents were supplied by Stago.