Does COVID Affect Clot Formation?

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Introduction

Covid infection is associated with an increased rate of thrombosis, with pulmonary emboli reported in 50% of critically ill patients[1].

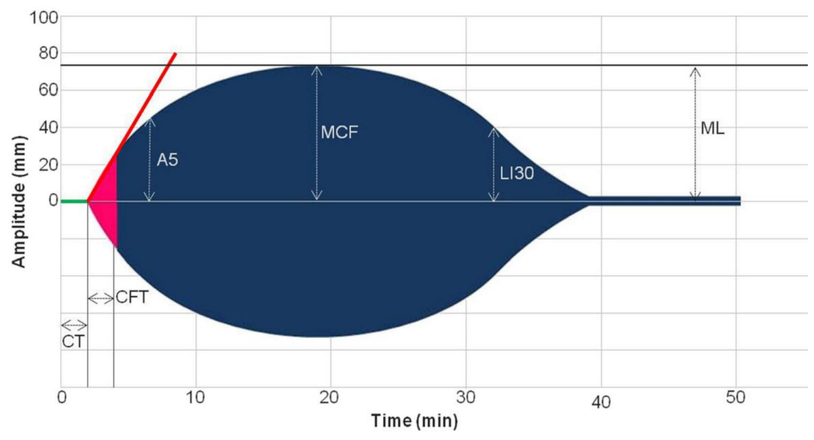
Rotem is a form of viscoelastic measurement of blood coagulation, allowing graphical representation of:

- the time a clot takes to form (clotting time (CT) and clotting formation time (CFT))
- clot strength (firmness of the clot after 5 min (A5) and maximum clot firmness (MCF))
- clot dissolution (maximum lysis (ML)).

It is becoming increasingly used to guide blood product usage in massive haemorrhage, for example in trauma, cardiac surgery and obstetrics.

Rotem provides four analyses for each sample:

- Intem (a measure of the intrinsic pathway, similar to the activated partial thromboplastin time)
- Extem (a measure of the extrinsic pathway, similar to the prothrombin time)
- Heptem (similar to Intem but excluding the effects of heparin)
- Fibtem (isolating fibrinogen function, to test the contribution of functional fibrinogen to clot formation).



In one study, Covid infection was associated with a reduced clotting time and an increased maximum clot firmness overall[2], but no difference in the Fibtem MCF value (fibrin strength) in Covid patients.

This study was to assess whether coagulation was affected by Covid infection in patients in our hospital.

Methods and Materials

Data from all Rotem analyses performed on patients on ICU (June 2020 to February 2021) were extracted, and analysed according to whether the patient had a positive Covid test within 28 days of admission to ICU. Corresponding laboratory tests of coagulation performed as near to the time of the Rotem analysis were also extracted.

Data were tested for normality by the Shapiro-Wilks test. Normal data were compared by the Student *t*-test; non-normal data were compared by the Mann-Whitney *U*-test. A *p*-value of less than 0.05 was taken as statistically significant. Correlation was assessed by Pearson co-efficients.

The following results were compared:

- Standard Rotem analyses in patients with and without Covid
- Fibrinogen concentrations and Fibtem MCF values, in patients with and without Covid.

Results

163 patients had Rotem analyses performed, of whom 12 (7.4%) had a positive Covid test. There was a significant increase in the clot strength (A5 and MCF) by the fibrin component between patients with and without Covid, but no other Rotem differences were found (**table 1**, and **figures 1** and **2**).

Moreover, we found a statistically significant difference between fibrinogen levels for Covid and non-Covid patients, suggesting a significant contribution of fibrinogen to clotting in Covid. And we demonstrated a strong positive correlation between fibrinogen levels and corresponding Rotem MCF values for all data (**figure 3**) and for Covid data (**figure 4**).

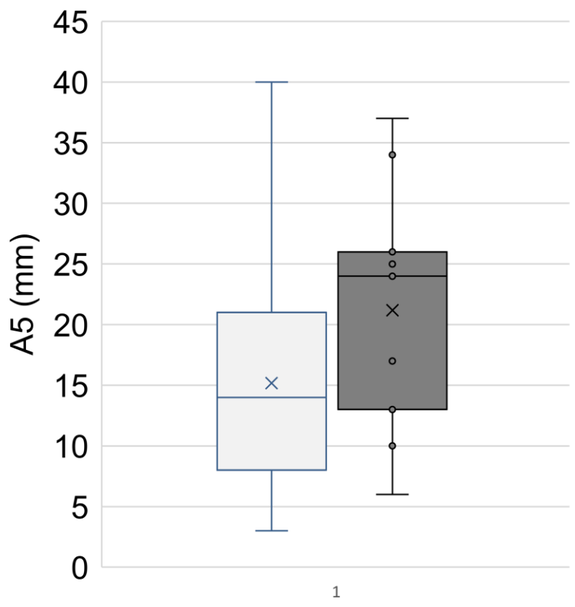


***Figure 1**. Differences in fibrin strength at 5 mins (A5) between patients without (light grey) and with (dark grey) Covid.*

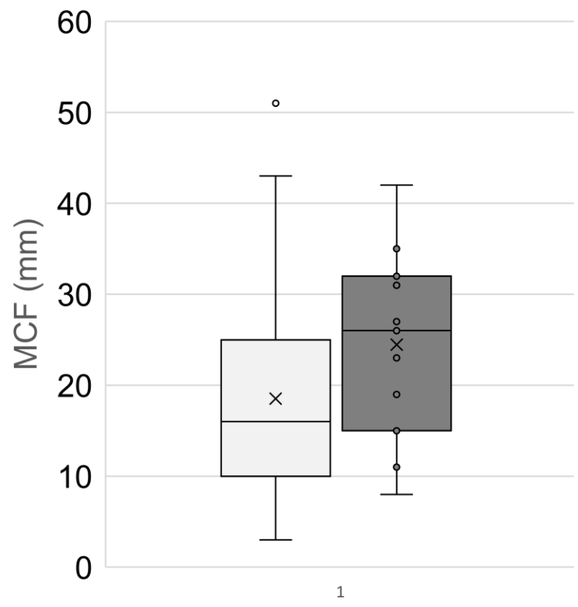


***Figure 2**. Differences in maximum clot firmness (MCF) due to the fibrin strength between patients without (light grey) and with (dark grey) Covid.*

	CFT (s)	CT (s)	A5 (mm)	MCF (mm)	ML (% of MCF)
Normal range[2]					
Fibtem				6–21	
Extem	46–149	53–83	32–52	55–72	<15
Intem	62–130	168–212	33–52	51–69	<15
Non-covid					
Fibtem	115 (32, 6378)	75 (48, 7699)	13 (3, 40)†	16 (3, 51)†	0 (0, 95)
Extem	69 (26, 712)	73 (46, 261)	48 (13, 78)	66 (24, 85)	5 (0, 91)
Intem	67 (27, 694)	182 (95, 640)	46 (12, 75)	63 (25, 83)	5 (0, 94)
Heptem	73 (26, 733)	179 (92, 620)	44 (11, 74)	63 (25, 84)	4 (0, 94)
Covid					
Fibtem	120 (41, 2634)	75 (52, 259)	21 (6, 37)†	25 (8, 42)†	0 (0, 0)
Extem	50 (29, 115)	75 (56, 260)	53 (34, 71)	69 (51, 81)	1 (7, 85)
Intem	60 (38, 161)	195 (119, 321)	50 (29, 67)	67 (46, 78)	8 (1, 78)
Heptem	60 (38, 176)	188 (119, 289)	50 (27, 62)	67 (44, 78)	7 (1, 62)

***Table 1.** Rotem characteristics for patients with and without Covid. Data are median (min, max). Key: † and highlighted: $p < 0.05$.*

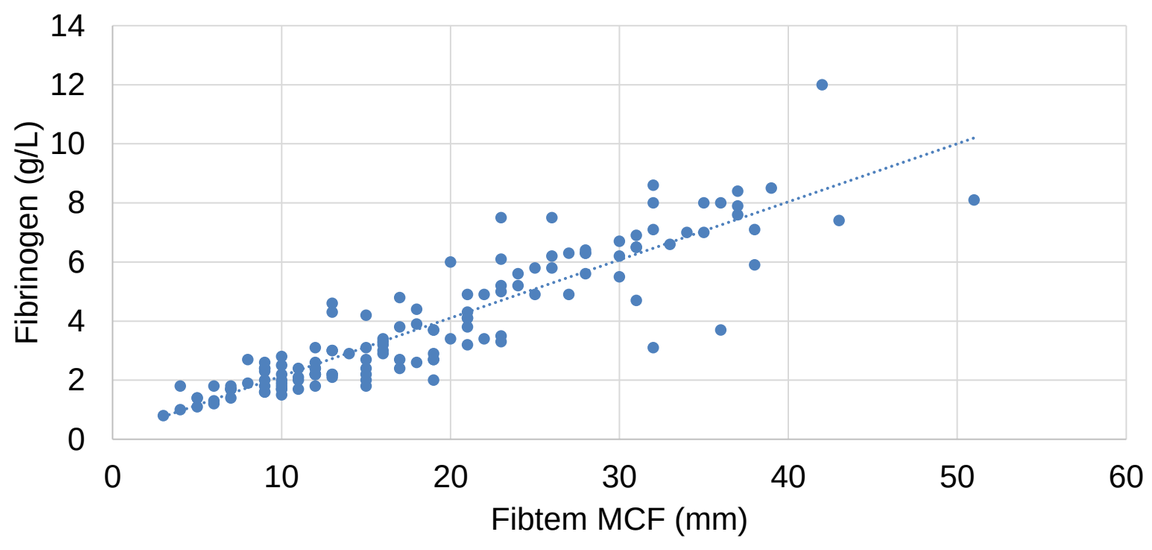


***Figure 3:** Correlation between fibrinogen levels and Fibtem maximum clot firmness (MCF) in all patients. $R^2 = 0.8105$, $p < 0.00001$.*

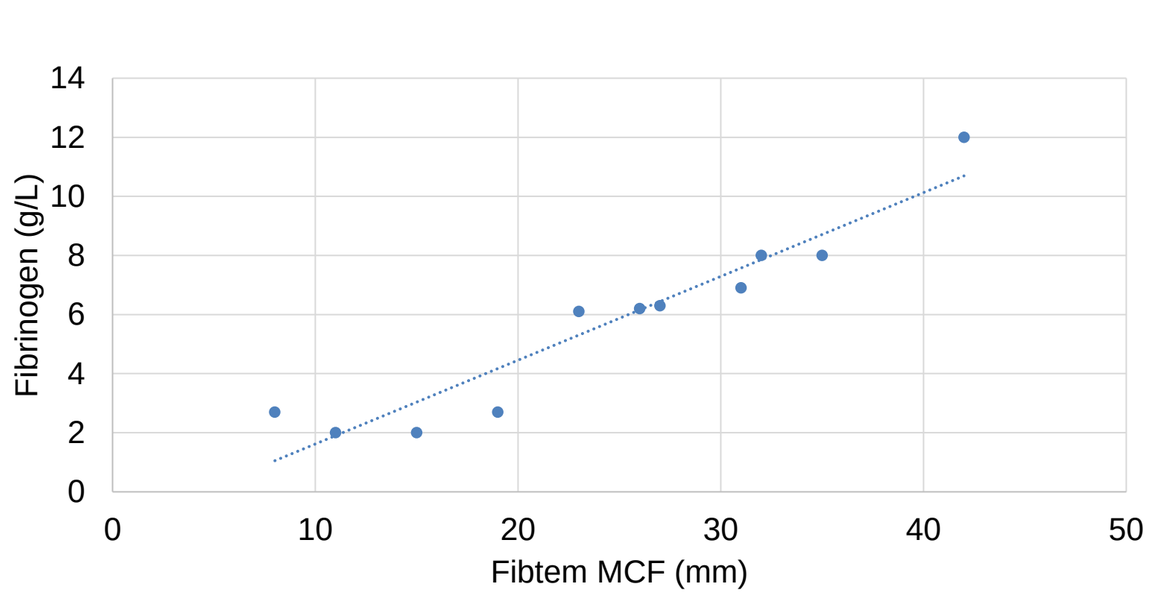


***Figure 4:** Correlation between fibrinogen levels and Fibtem maximum clot firmness (MCF) in Covid patients. $R^2 = 0.905$, $p < 0.00001$.*

Conclusions

There was a significant increase in the clot firmness due to the fibrin component in patients with Covid infection, compared with those without. This is at variance with previous studies, which have found no difference. The strength of the fibrin component showed strong correlation with the fibrinogen level. There were no other differences detected.

The study may be limited by small numbers of patients, and the heterogeneity of the patients within each group.

References

1. Bompard F, Monnier H, Saab I, et al. Pulmonary embolism in patients with COVID-19 pneumonia. Eur Respir J 2020; 56: 2001365. doi.org/10.1183/13993003.01365-2020.
2. van Veenendaal N, Scheeren TWL, Meijer K, van der Voort PHJ. Rotational thromboelastometry to assess hypercoagulability in COVID-19 patients. Thromb Res. 2020; 196: 379-381. doi:10.1016/j.thromres.2020.08.046.