Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Screening of COVID-19-associated hypercoagulopathy using rotational thromboelastometry

Coronavirus disease 2019 (COVID-19) is caused by the novel virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease has now spread worldwide, causing a pandemic.

According to Klok et al., complications such as coagulopathy have previously been reported in critically ill COVID-19 patients, with around 30% of critically ill COVID-19 patients developing thrombotic complications [1]. Without appropriate assessment and treatment, physicians may not be able to improve outcomes in these patients, even with the use of invasive therapies such as mechanical ventilation and extracorporeal membrane oxygenation.

Assessment of coagulopathy, especially hypercoagulopathy, is difficult to achieve through conventional coagulation tests, which include measurement of platelet count, activated partial thromboplastin time (APTT), prothrombin time (PT), d-dimer levels, and fibrinogen levels. Viscoelastic hemolytic assays (VHA), such as thromboelastography (TEG), (TEG®; Haemonetics Co., Braintree, MA, USA) and rotational thromboelastometry (ROTEM), (ROTEM®; TEM International FZC, Munich, Germany) are more reliable for the detection of coagulopathy than conventional coagulation tests, but are not commonly used [2].

Based on the TEG data of COVID-19 patients who were admitted to intensive care units (ICU), Mauro et al. reported that coagulopathy in severe COVID-19 patients was not disseminated intravascular coagulation, but was hypercoagulopathy with high d-dimer values [3]. However, some COVID-19 patients may show a hypercoagulable pattern on VHA testing and have normal conventional coagulation test results.

A 57-year-old woman with COVID-19 was transferred to our ICU due to her critically ill condition with typical pneumonia diagnosed by polymerase chain reaction (PCR) and chest computed tomography (CT). She required endotracheal intubation due to hypoxia and a low PaO_2/FiO_2 ratio of 120.

Contrast-enhanced CT did not suggest thrombotic complications. Furthermore, conventional coagulation test results obtained on the first day of ICU admission revealed near normal values, except for slightly elevated d-dimer levels (Table 1). A ROTEM examination (Fig. 1) revealed that the maximum clot firmness values in EXTEM and INTEM were 73 mm and 68 mm, respectively, and the clot formation time (CFT) in FIBTEM was 54 s. These findings were suggestive of hypercoagulopathy. Unfractionated heparin was started at a dose of 10,000 U/day as continuous intravenous infusion for prophylaxis of thrombotic complications.

The infusion rate of unfractionated heparin was adjusted to maintain an APTT of 50–80 s. However, ROTEM data still indicated a hypercoagulable state (Fig. 1). Additionally, the HEPTEM and INTEM data were similar every day, suggesting that the heparin anticoagulant therapy was ineffective. Nevertheless, the patient improved due to prone ventilation and was extubated on the seventh day of admission.

COVID-19 can lead to development of a hypercoagulopathy that may not be seen with conventional tests of coagulation, but can be detected through ROTEM. Thus, robust anticoagulant therapy might be needed to prevent thrombotic complications in a particular subset of COVID-19 patients.

Alexander et al. conducted a study that involved patients who developed thrombotic complications after major abdominal surgeries [4]. Upon ROTEM testing, these patients exhibited a mean CFT in FIBTEM of 378.9 s while the CFT in our patient was 54 s.

The CFT in FIBTEM cannot be measured in a healthy person's blood because the FIBTEM includes cytochalasin D, which strongly inhibits the function of platelets and polymerization of fibrinogen. However, the FIBTEM column confirmed that our patient was in a hypercoagulable state. VHA screening may be necessary for COVID-19 patients. If our patient had not undergone ROTEM testing, her hypercoagulopathy might have remained undetected, and timely prophylaxis in the form of adequate unfractionated heparin would not have been administered, which could have led to potentially fatal thrombotic complications.

We obtained consent from the patient to publish this paper.

Author statement

YI, TS, and MY conceived the article. All authors contributed to the writing of the manuscript. DK, KS and TA supervised the investigation. KO, HK, HB, and KT were involved in the clinical management of the patient. All authors interpreted the results and participated in discussions. YI drafted the initial manuscript and all authors contributed substantially to its revision. All authors read and approved the final version of the manuscript. YI takes primary responsibility for the entire paper.

Table 1
Results of standard laboratory examinations 1, 2, and 6 days after admission.

Examination	Day 1	Day 2	Day 6
PT-INR	0.92	0.92	0.93
APTT (s)	37.3	63.3	48.2
Fibrinogen (mg/dL)	334	372	425
FDP(μg/mL)	4.7	5.4	4.7
D-dimer (μg/mL)	1.5	1.8	1.9
AT3 (%)	86	86	110
Platelet count (10^4/μL)	20.3	21.2	31.7
White blood cells (/μL)	4100	7300	3900
C-reactive protein (mg/dL)	3.91	7.54	2.26

PT-INR: prothrombin time - international normalized ratio, APTT: activated partial thromboplastin time, FDP: fibrin/fibrinogen degradation products, AT3: anti-thrombin 3.

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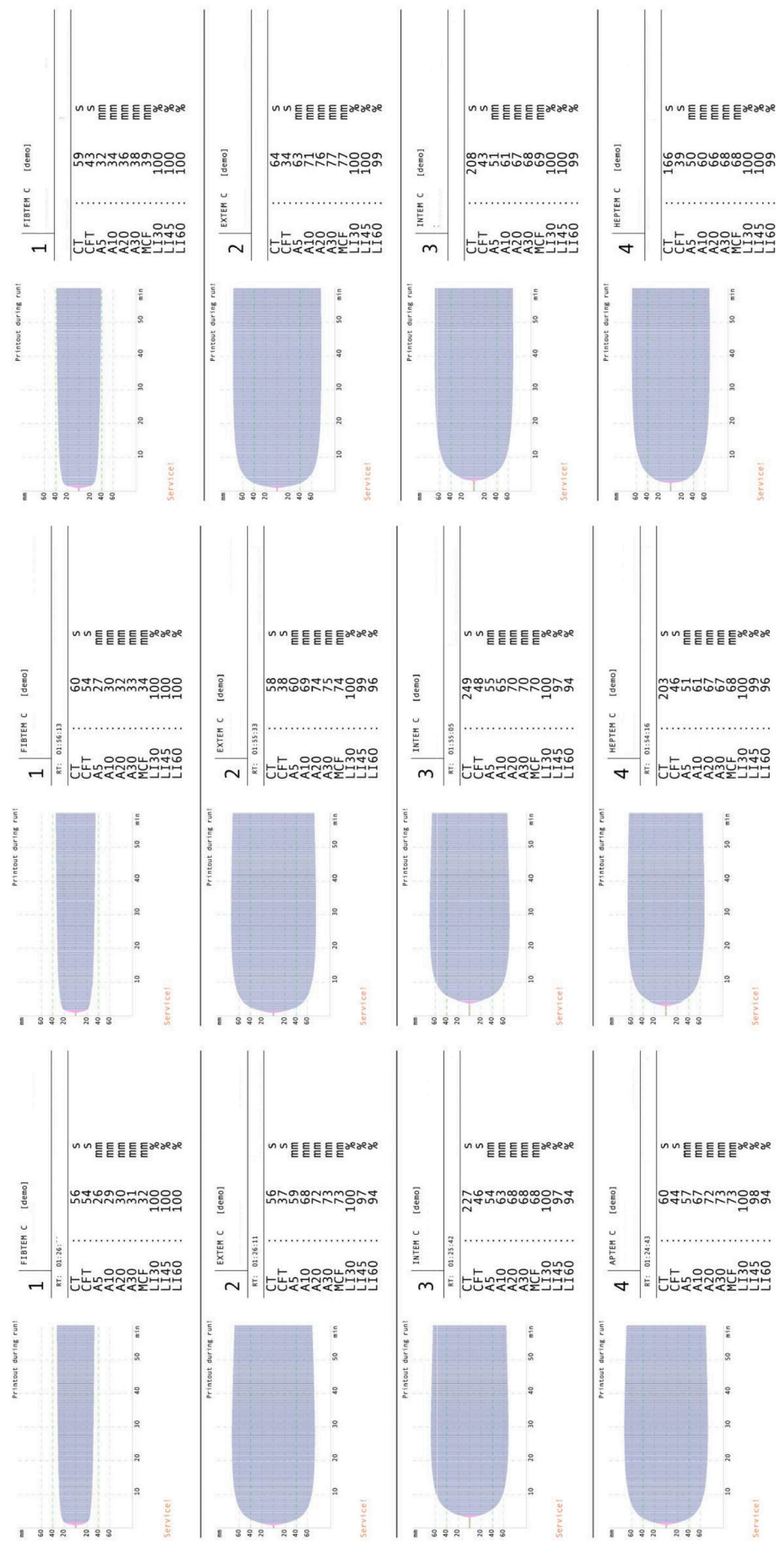

Fig. 1. Patient's ROTEM data on days 1, 2, and 6 in the ICU. On day 1, an APTEM column was used to evaluate fibrinolysis parameters. Clotting time was very short for each parameter, and the width of the clot was significantly more. The CFT in FIBTEM was 54 s. These results suggested hypercoagulopathy.
Unfractionated heparin was administered and the HEPTEM column was used to evaluate the treatment efficiency on second and sixth days. This data indicate that the patient's hypercoagulopathy did not resolve even after unfractionated heparin was administered. CFT: clot formation time, ICU: intensive care unit, ROTEM: rotational thromboelastometry.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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