Viscoelastic Coagulation Monitor (VCM) as a novel device to assess coagulation at the bedside. A single-center experience during the COVID-19 pandemic.

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Supplementary material

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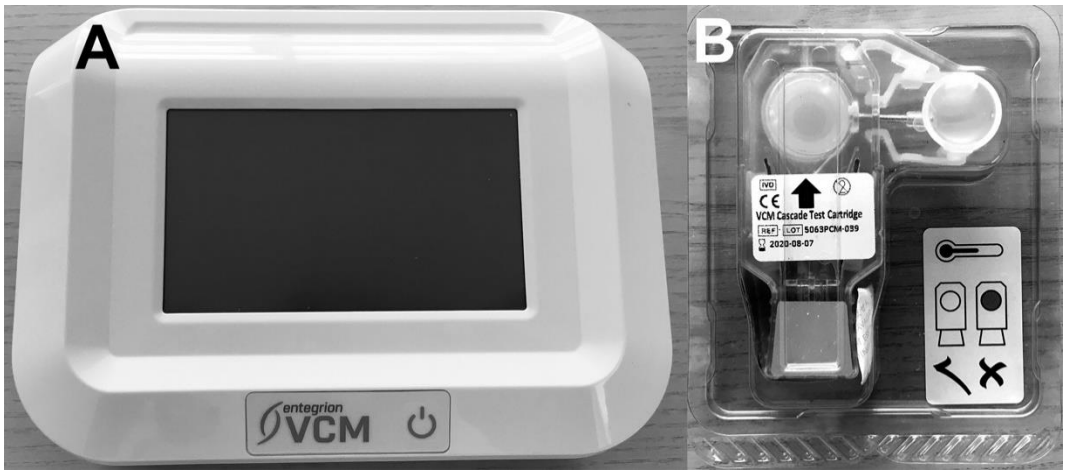
Figure E1. Panel A: VCM device. Panel B: disposable cartridge.

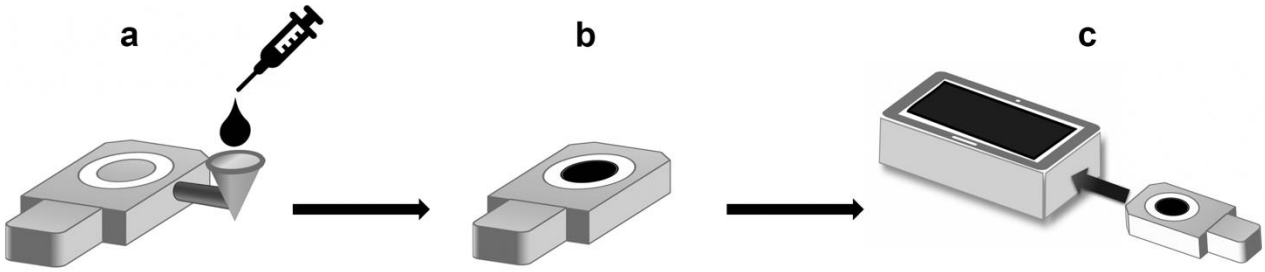


VCM (Viscoelastic Coagulation System, Entegrion, Durham, NC, USA) was employed at the same time of TEG for patient testing. This system is made of an analyzer, disposable cartridges and a heater plate, which is used to warm the cartridges at 37°C during the pre-test phase.

Description of the analytical procedure:

Quality check was run following manufacturer's advice. Upon blood withdrawal, a small unmetered sample of blood was added to the cartridge through an additional cup (Figure E2, a); automatically, the right amount of blood flows to fill the cartridge between two glass surfaces (Figure E2, b). The additional cup is then removed, the lateral port is closed and the cartridge is inserted in the analyzer to run the test (Figure E3, c). The environment inside the analyzer is continuously kept at constant temperature and humidity.

Figure E2. Panel A: VCM device. Panel B: disposable cartridge.

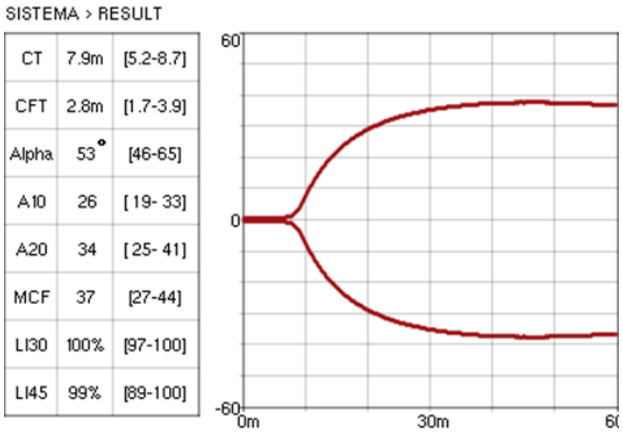


VCM analysis procedure as pointed out in *Description of the analytical procedure*.

Figure E3. Examples of VCM tracings

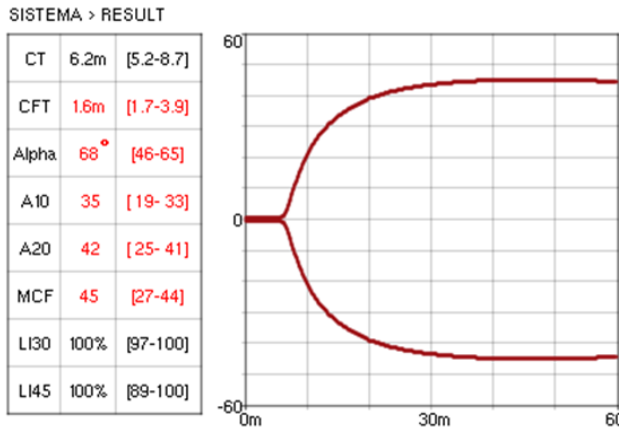
a. Normal

Normal platelet count (3.7 *10^5/µL), Normal fibrinogen (4.8 g/L), Normal D-dimer (3.3 mcg/ml). On LMWH (Clexane 8000 IU bid)



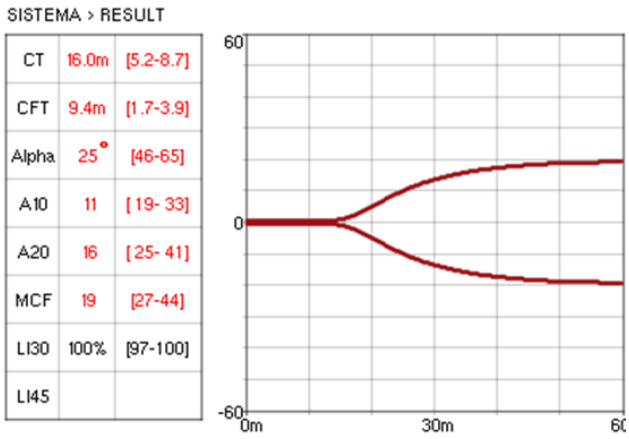
b. Hypercoagulable

High platelet count (5.1 *10^5/µL), High fibrinogen (6.6 g/L), Slightly elevated D-dimer (1.2 mcg/ml). On LMWH (Clexane 8000 IU bid)



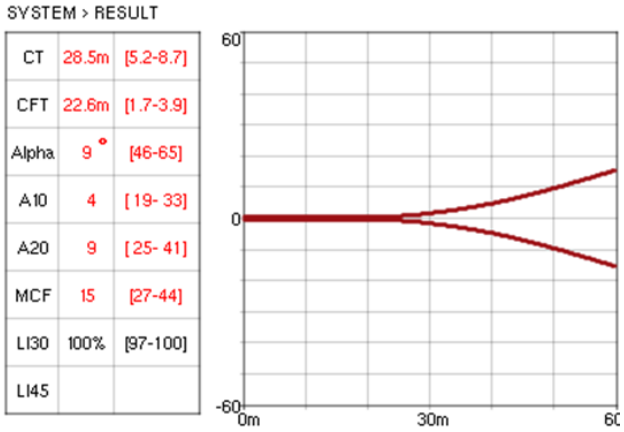
c. Hypocoagulable

i) Low platelet count (8*10^5/µL), normal fibrinogen (3 g/L), slightly elevated D-dimer (1.1 mcg/ml). No heparin.



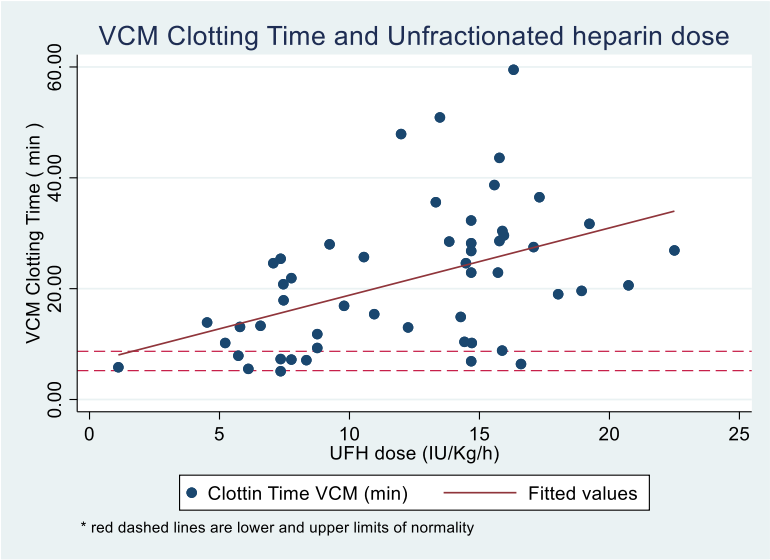
ii) Effect of UFH (unfractionated heparin).

Low platelet count (88*10^5/µL), normal fibrinogen (4.2 g/L), Elevated D-dimer (44 mcg/ml). On UFH (24 IU/Kg/h) in ECMO



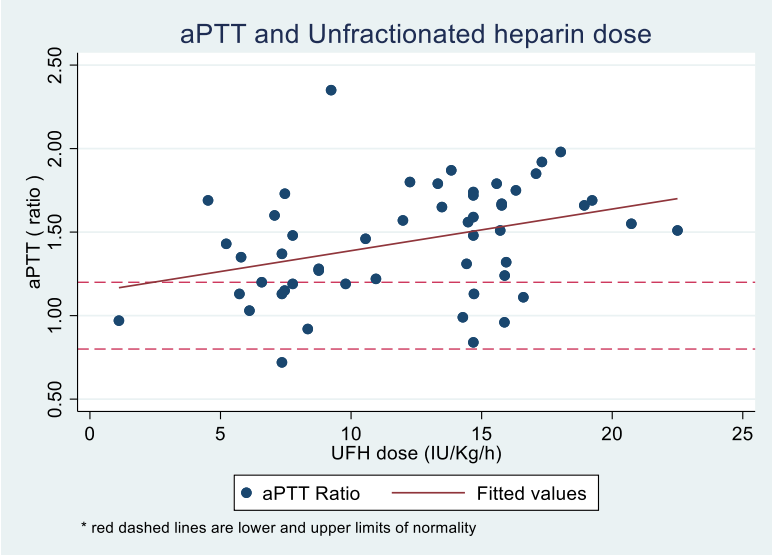
CT, Clotting Time; CFT, Clot Formation Time; Alpha, angle; A10, Amplitude at 10 minutes; A20, Amplitude at 20 minutes; MCF, Maximum Clot Firmness; LI30, Lysis at 30 minutes; LI45, Lysis at 45 minutes.

Figure E4. Correlation and linear fit of VCM CT and aPTT with UFH dose.



Number of obs = 52

Spearman's rho = 0.48, p = 0.00034



Number of obs = 52

Spearman's rho = 0.35, p = 0.010

Table EI. Summary of the parameters reported by the VCM system (from the operator's manual).

Parameter	***Unit***	***Description***
CT (Clotting Time)	Seconds	The time from the start of the test until the amplitude of 1% above the baseline has been reached, where the slot starts to form
CFT (Clot Formation Time)	Seconds	The time between 1% and 10% amplitude of the clotting signal, describing the kinetics of the clot
Alpha (Alpha-Angle)	Degrees (°)	The angle between the time axis and the tangent to the clotting curve at an amplitude of 1%, describing the kinetics of the clot
A10 & A20 (Amplitude at 10 and 20 minutes)	VCM Units	Clot amplitude at 10 and 20 minutes, describing clot firmness
MCF (Maximum Clot Firmness)	VCM Units	The firmness and quality of the clot, described by the maximum amplitude that is reached before the beginning of fibrinolysis
LI30 & LI45 (Lysis Index at 30 and 45 minutes)	%	Amplitude of the clot at 30 and 45 minutes, described as a percentage of the MCF

Table EII. Blood count, coagulation, biochemistry and VCM parameters on the first day of ICU admission

Variable	***Reference limits***	***Median (25^{th}-75^{th})***	***Min***	***Max***	***N***
Laboratory parameters					
Hb (g/dL)	*12.0 - 15.5*	10.6 (10.3 - 10.8)	10.1	11.1	4
WBC ($10^3/mm^3$)	*4.0 - 11.0*	11.5 (6.3 - 16.9)	4.0	19.5	4
Creatinine (mg/dL)	*0.6 – 1.2*	0.6 (0.6 - 1.0)	0.6	1.3	4
Bilirubin (mg/dL)	*0.1 – 1.2*	0.5 (0.4 - 1.1)	0.4	1.8	4
AST (mg/dL)	*10 - 40*	32.5 (8.0 - 57)	8.0	57	2
ALT (mg/dL)	*7 - 56*	44 (36 – 77)	34	104	4
g-GT (mg/dL)	*9 - 48*	141 (74 – 285)	33	403	4
LDH (mg/dL)	*140 - 280*	311 (180 – 425)	118	472	4
Ferritin (ng/mL)	*12 - 300*	356.5 (184.5- 1183)	142	1880	4
CRP (mg/dL)	*0 - 10*	0.8 (0.2 - 5.3)	0.1	9.2	4
PT ratio	*0.8 - 1.2*	1.0 (1.0 - 1.1)	0.9	1.1	4
aPTT ratio	*0.8 - 1.2*	0.9 (0.9 - 1.1)	0.9	1.1	4
Fibrinogen (g/L)	*2 – 4*	2.3 (1.9 - 4.6)	1.7	6.7	4
D-dimer (mcg/mL)	*<0.5*	0.5 (0.2 - 1.1)	0.2	1.5	4
Platelet count (10^5/µL)	*1.5 - 4*	1.7 (1.4 - 2.0)	1.2	2.3	4
VCM parameters					
Clotting Time, CT (min)	*5.2 – 8.7*	7.8 (6.7 - 9.1)	6.5	9.7	4
Clot formation time, CFT (min)	*1.7 – 3.9*	4.3 (3.1 - 4.5)	2.0	4.7	4
Angle, Alpha (degrees)	*46 - 65*	42.5 (39.5 - 53)	38	62	4
Amplitude 10 min, A10 (mm)	*19 - 33*	20 (18.5 - 27.5)	18	34	4
Amplitude 20 min, A20 (mm)	*25 – 41*	27 (25 – 35.5)	25	42	4
Maximum clot firmness, MCF (mm)	*27 - 44*	32 (29 – 39.5)	27	46	4
Lysis at 30 min, Li30 (%)	*97 - 100*	100 (100 – 100)	100	100	4

Data are shown as median (25th – 75th). N, number of observations; LDH, lactate dehydrogenase; CRP, C-reactive protein; Hb, hemoglobin; WBC, white blood cells count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; g-GT, g-glutammil transpeptidase, PT, prothrombin time; aPTT, activated partial thromboplastin time.

Table EIII. Correlation between VCM parameters and Ferritin and C-Reactive protein as markers of inflammation

	Ferritin			C-Reactive Protein		
Variables	Spearman's rho	P value	N	Spearman's rho	P value	N
CT	0.42	0.0000	149	0.38	0.0000	148
CFT	0.34	0.0000	149	0.19	0.0197	148
Alpha	-0.37	0.0000	145	-0.28	0.0006	144
A10	-0.32	0.0001	147	-0.06	0.4743	146
A20	-0.35	0.0000	145	-0.02	0.8204	144
MCF	-0.34	0.0000	148	0.01	0.8537	147
Li30	0.10	0.2528	139	0.04	0.6402	138
Li45	0.08	0.4307	109	-0.03	0.7489	108

CT = Clotting Time (min); CFT = Clot formation time (min); Alpha = Angle (degrees); A10 = Amplitude at 10 min (mm); A20 = Amplitude at 20 min (mm); MCF = Maximum Clot Firmness (mm); Li30 = Lysis at 30 min (%); Li45 = Lysis at 45 min (%)

Table EIV. Description of thrombotic and hemorrhagic episodes.

Site of Thrombosis	***Number of patients. (%)***
Pulmonary Embolism	5 (13.9)
Deep Vein Thrombosis	5 (13.9)
Pulmonary Embolism and Deep Vein Thrombosis	2 (5.6)
Internal Jugular Vein Thrombosis	1 (2.8)
Pulmonary Embolism, Deep Vein Thrombosis and Internal Jugular Vein Thrombosis	1 (2.8)
Total	*14/36 (38.9)*
Site of Hemorrhage	
Gluteal artery	1 (2.8)
Hemoptysis and rectal	1 (2.8)
Epistaxis	1 (2.8)
Glottic	1 (2.8)
ECMO cannula	1 (2.8)
Uterine	1 (2.8)
Oral	1 (2.8)
Oral and Pleural	1 (2.8)
Oral and Rectal	2 (5.6)
Petechiae CNS	1 (2.8)
Rectal	1 (2.8)
Tracheal	1 (2.8)
Total	*13/36 (26.1)*

Table EV. Receiver Operating Characteristics (ROC) curves of VCM parameters and three hypercoagulable patterns.

a) Platelet count > $4*10^5/\mu L$

VCM variable	Ref limits	Obs	ROC (95%CI)	Estimated cut point	Sensitivity at cut point	Specificity at cut point	ROC Area at cut point
Clotting Time, CT (min)	5.2-8.7	99	0.28 (0.17-0.40)	.	0	1	0.5
Clot formation time, CFT (min)	1.7-3.9	99	0.11 (0.02-0.19)	.	0	1	0.5
Angle, Alpha (degrees)	46-65	99	0.89 (0.81-0.97)	62.8	0.86	0.85	0.85
Amplitude 10 min, A10 (mm)	19-33	99	0.85 (0.76-0.94)	33.6	0.82	0.82	0.82
Amplitude 20 min, A20 (mm)	25-41	99	0.85 (0.75-0.94)	40.3	0.82	0.81	0.81
Maximum clot firmness, MCF (mm)	27-44	98	0.84 (0.75-0.94)	41.2	0.86	0.77	0.81

b) fibrinogen > 4 g/L

VCM variable	Ref. limits	Obs	ROC	Estimated cut point	Sensitivity at cut point	Specificity at cut point	ROC Area at cut point
Clotting Time, CT (min)	5.2-8.7	98	0.55 (0.44-0.67)	8.4	0.53	0.61	0.57
Clot formation time, CFT (min)	1.7-3.9	98	0.35 (0.24-0.46)	1.2	1	0.04	0.52
Angle, Alpha (degrees)	46-65	98	0.59 (0.48-0.71)	51.5	0.81	0.38	0.60
Amplitude 10 min, A10 (mm)	19-33	98	0.74 (0.64-0.84)	28.6	0.70	0.69	0.69
Amplitude 20 min, A20 (mm)	25-41	98	0.73 (0.63-0.83)	36.7	0.64	0.75	0.69
Maximum clot firmness, MCF (mm)	27-44	97	0.76 (0.66-0.85)	40.8	0.62	0.82	0.72

c) Combination of fibrinogen > 4 g/L and six-fold upper reference limit of D-dimer

VCM variable	Ref. limits	Obs	ROC	Estimated cut point	Sensitivity at cut point	Specificity at cut point	ROC Area at cut point
Clotting Time, CT (min)	5.2-8.7	89	0.70 (0.40-0.99)	11.6	0.6	0.89	0.75
Clot formation time, CFT (min)	1.7-3.9	89	0.64 (0.32-0.96)	3.75	0.6	0.82	0.71
Angle, Alpha (degrees)	46-65	89	0.35 (0.02-0.67)	63.5	0.4	0.70	0.55
Amplitude 10 min, A10 (mm)	19-33	89	0.37 (0.10-0.63)	.	0	1	0.5
Amplitude 20 min, A20 (mm)	25-41	89	0.38 (0.11-0.64)	19	1	0.02	0.51

Maximum clot firmness, MCF (mm)	27-44	88	0.48 (0.28-0.68)	33.5	1	0.26	0.63

Receiver operating characteristic (ROC) curves comparing accuracy of various VCM parameters for: a) Platelet count above upper reference limit (> $4*10^5/\mu L$); b) fibrinogen above upper reference limit (> 4 g/L); c) hypercoagulable state defined as the fibrinogen > 4 g/L and six-fold upper reference limit of D-dimer (i.e. 3 mcg/mL)[23]. ROC and 95% confidence interval (CI) are shown in the graphs. For each variable, an empirical cut point (Youden method) for the detection of hypercoagulability was estimated, with its sensitivity, specificity and ROC area at the cut point. ROC curves were computed on samples of patients non receiving UFH. VCM=Viscoelastic Clotting Monitoring.