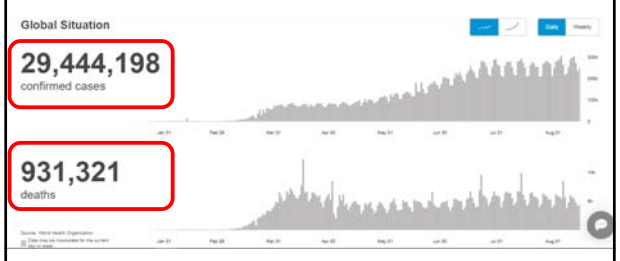
GÖĞÜS KALP Ddamar ANESTEZİ VE YOĞUN BAKIM DERNEĞİ 26. ULUSAL KONGRESİ 17-18 Eylül 2020 E-KONGRE

Dr. Onat BERMEDE, DESA

Ankara Üniversitesi Tıp Fakültesi
Anesteziyoloji ve Reanimasyon AD

https://covid19.who.int/



https://covid19.who.int/

Immunomodulators in COVID-19 - Two Sides to Every Coin

[1,2] Timothy AC Snow, MBBS BSc, [1,2] Mervyn Singer, MD, FRCP, [1,2] Nishkantha Arulkumaran, PhD,

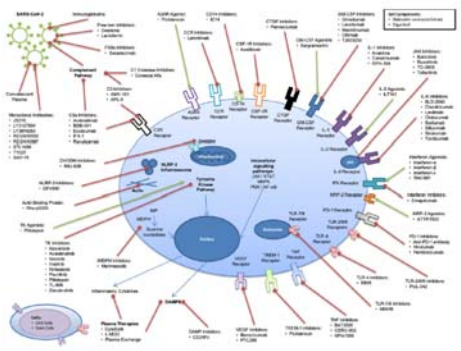


Figure 1: Summary of biological therapies undergoing randomised controlled trials in COVID-19

UYGUNLUK

- Optimal MV ayarlarına rağmen hipoksemik ?
- Nöromuskuler blokaj / Prone pozisyon ?
- Altta yatan hastalık reversible ?

→ EVET

KONTRENDİKASYON

- Uzun süreli MV'ye bağlı hasar?
- Yüksek hemorajik komplikasyon riski?
- Kanülasyon için uygun olmayan vasküler yapı?
- Normal/hiperdinamik LV varlığında distribütif şok?

KISA DÖNEM SAĞKALIM

- Altta yatan hastalık nedeniyle kötü prognoz?
- Sağkalım skorları kötü mü?
- Komorbiditeye bağlı sağkalım 5 yıldan az mı?

HAYIR

HAYIR → **MULTİDİSİPLİNER TAKIM KARARI**

CHEST 2020; 158(3):1036-1045

MULTİDİSİPLİNER TAKIM KARARI

↓ EVET

HEMODİNAMİK DEĞERLENDİRME / EKOKARDİYOGRAFİ

Ciddi LV disfonksiyonu?

EVET → **VA ECMO**

HAYIR → **VV ECMO**

CHEST 2020; 158(3):1036-1045

COVID-19 and ECMO: the interplay between coagulation and inflammation—a narrative review

Kowalewska et al. Critical Care (2020) 24:205
https://doi.org/10.1186/s13054-020-02925-3

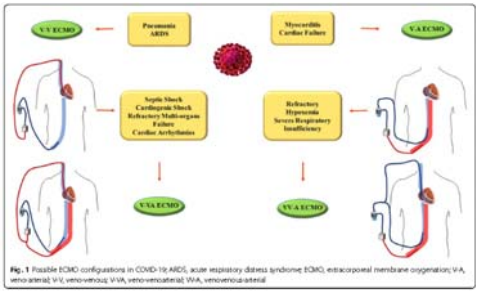


Fig. 1 Possible ECMO configurations in COVID-19 ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation; V-A, veno-arterial; V-V, veno-venous; V-VA, veno-venoarterial; VV-A, venovenous-arterial

---

EuroELSO COVID-19 Survey

EuroECMO-COVID

Survey 14 September 2020

Age and Gender Distribution in ECMO – COVID-19

	21 March	28 March	04 April	11 April	18 April	25 April	02 May	09 May	17 May
Mean Age	50.5	53.5	51.9	52.5	52.4	52.2	52.2	52.3	52.2
Min Age	20	16	16	16	16	16	16	16	16
Max Age	73	74	74	74	78	78	79	79	79
% Male	90	80	79	81	80	80	80	79	79
% Female	10	20	21	19	20	20	20	21	21

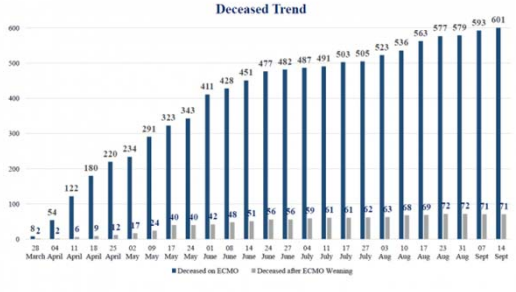
	24 May	01 June	08 June	14 June	24 June	27 June	04 July	11 July	17 July
Mean Age	52.4	52.4	52.4	52.5	52.5	52.5	52.5	52.5	52.3
Min Age	16	16	16	16	16	16	16	16	16
Max Age	79	79	79	80	80	80	80	80	80
% Male	78	78	78	78	78	78	78	79	79
% Female	22	22	22	22	22	22	22	21	21

	27 July	03 August	10 August	17 August	23 August	31 August	07 September	14 September
Mean Age	52.3	52.4	52.4	52.5	52.6	52.6	52.6	52.6
Min Age	16	16	16	16	16	16	16	16
Max Age	80	80	80	80	80	80	80	80
% Male	78	78	78	78	78	78	78	79
% Female	22	22	22	22	22	22	22	21

EuroECMO-COVID

Survey 14 September 2020

Deceased Trend

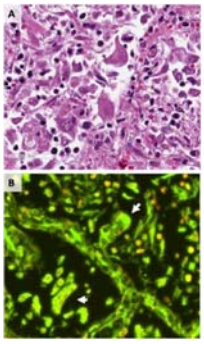


Status n.a. 10 patients

COVID-19 update: Covid-19-associated coagulopathy

Richard C. Becker[1]

Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02134-3



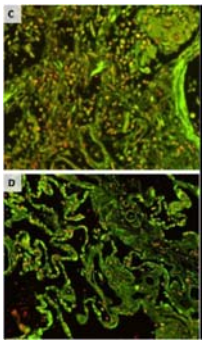
Alveoler hasar, sitolojik atipi

Ekstraselüler DNA (kırmızı) ve RNA (yeşil)

COVID-19 update: Covid-19-associated coagulopathy

Richard C. Becker[1]

Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02134-3



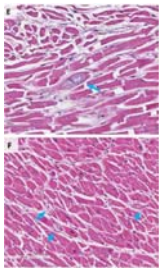
Fibrin ve ekstrasellüler nükleik asitler

Yıkım

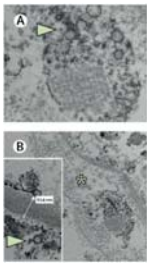
COVID-19 update: Covid-19-associated coagulopathy

Richard C. Becker[1]

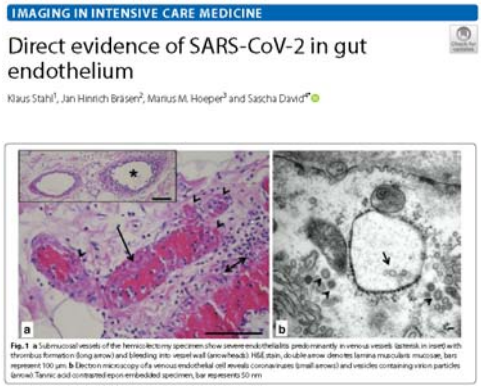
Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02134-3



Kardiyomiyositlerde dejenerasyon



Glomerüllerde viral partiküller

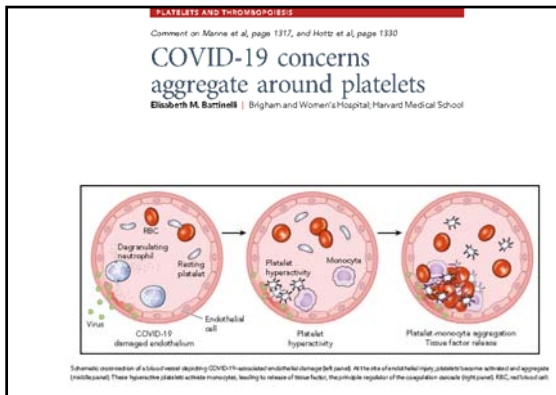


IMAGING IN INTENSIVE CARE MEDICINE

Direct evidence of SARS-CoV-2 in gut endothelium

Klaus Stahl[1], Jan Hinrich Bräsen[2], Marius M. Hoeper[3] and Sascha David[4]*

Fig. 1 a Submucosal vessels of the hemicolectomy specimen show severe endotheliitis predominantly in venous vessels (asterisk in inset) with thrombus formation (long arrow) and bleeding into vessel wall (arrowheads). H&E stain, double arrow denotes lamina muscularis mucosae, bars represent 100 µm. b Electron microscopy of a venous endothelial cell reveals coronaviruses (small arrows) and vesicles containing virion particles (arrow). Tannic acid-contrasted epon-embedded specimen, bar represents 50 nm



PLATELETS AND THROMBOPOIESIS

Comment on Manne et al, page 1317, and Hottz et al, page 1330

COVID-19 concerns aggregate around platelets

Elisabeth M. Bertinelli | Brigham and Women's Hospital, Harvard Medical School

COVİD 19 İlişkili Koagülopati

- Fibrinojen ve D-dimer artışı
- PT, aPTT ve Plt minimal değişiklik
- IL-6 seviyeleri fibrinojen ile korele
- Koagülopati hastalık şiddeti ve tromboinflamasyon ile ilişikili iken intrinsik viral aktivite ile değil
- Başvuruda D-dimer yüksekliği artmış mortalite
- D-dimer artışı multiorgan yetmz ve DIC için kötü prognoz

Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135(23):2033-2040.

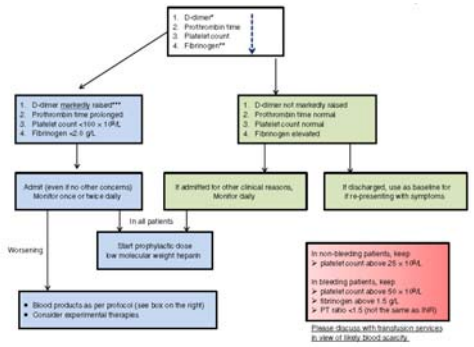
COVID-19 update: Covid-19-associated coagulopathy

Richard C. Becker[1]

Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02134-3

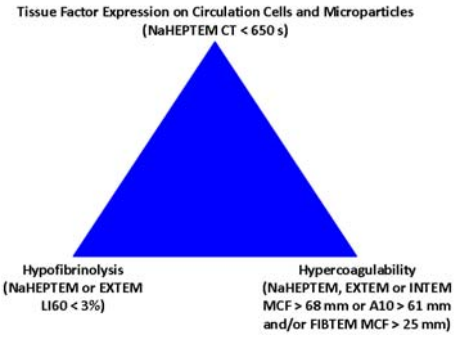
	DIC	Microangiopathy	Covid-19
PT	↑↑	--	↑↑
PTT	↑↑	--	↑
Fibrinogen	↓	--	↑↑
FDPs	↑↑	--	↑↑
D-dimer	↑	--	↑↑ or ↑+
Platelet count	↓↓	↓	↑ or --
Peripheral blood Smear++	+	++	+
VWF	↑↑	--	↑↑
ADAMTS 13		↓	--
AT	↓	↓	↑
ACA	--	--	+
PC	↓	--	+

ISTH interim guidance on recognition and management of coagulopathy in COVID-19



Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. J Thromb Haemost. 2020;18(5):1023-1026.

ROTEM Triad of Thrombosis



CRITICAL CARE

Rotational thromboelastometry predicts thromboembolic complications after major non-cardiac surgery

Alexander Hincker, Justin Feit, Robert N Sladen and Gebhard Wagener[1]

Hincker et al. Critical Care 2014, 18:549
http://ccforum.com/content/18/5/549

Table 1 Preoperative rotational thromboelastometry (ROTEM) parameters

ROTEM parameter	Normal values	No thromboembolic complication	Thromboembolic complication	P-value	AUC ROC
EXTEM					
Clotting time, s	42 to 74	55.1 (31.2)	48.7 (16.9)	0.19	---
Clot formation time, s	46 to 148	87.1 (61.7)	58.5 (16.6)	<0.001	0.74
Alpha angle, degrees	63 to 81	74.3 (6.9)	78.4 (3.1)	0.032	0.70
Amplitude at 10/20 minutes, mm	50 to 69	58.2 (8.7)	64.0 (5.4)	0.038	0.72
Maximum clot firmness, mm	49 to 71	65.0 (7.5)	70.4 (5.2)	0.029	0.73
INTEM					
Clotting time, s	137 to 246	171.5 (34.1)	165.8 (24.6)	0.11	---
Clot formation time, s	71 to 82	72.2 (57.3)	51.0 (11.4)	<0.001	0.75
Alpha angle, degrees	52 to 72	76.5 (5.5)	79.4 (2.4)	0.006	0.72
Amplitude at 10/20 minutes, mm	137 to 246	56.7 (7.8)	60.0 (5.8)	0.012	0.75
Maximum clot firmness, mm	52 to 72	62.8 (7.1)	68.6 (6.0)	0.02	0.74
FIBTEM					
Clotting time, s	43 to 69	53.3 (47.4)	44.7 (13.1)	0.11	---
Clot formation time, s		339.9 (366.5)	378.9 (606.0)	0.12	---
Alpha angle, degrees		73.6 (8.6)	77.0 (5.4)	0.085	---
Amplitude at 10/20 minutes, mm	8 to 21	16.5 (6.8)	23.7 (11.2)	0.010	---
Maximum clot firmness, mm	9 to 25	17.8 (7.6)	24.8 (11.2)	0.015	---

For significant predictive tests, the area under the curve (AUC) of the receiver operating characteristic (ROC) curve is listed. EXTEM, extrinsic rotational thromboelastometry; INTEM, intrinsic rotational thromboelastometry; FIBTEM, fibrinogen rotational thromboelastometry; ns, not significant.

Thromboelastometry hypercoagulable profiles and portal vein thrombosis in cirrhotic patients with hepatocellular carcinoma

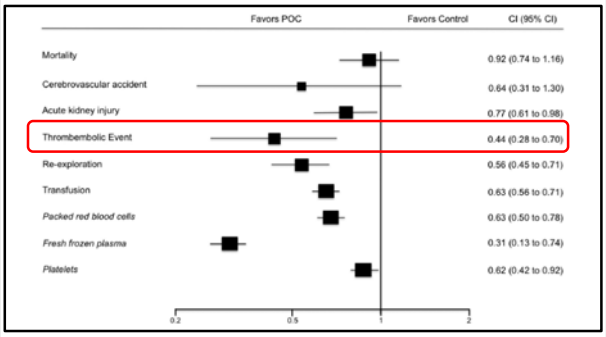
Alberto Zanetto[a,1], Marco Senzolo[a,*,1], Alessandro Vitale[b], Umberto Cillo[b], Claudia Radu[c], Francesca Sartorello[c], Luca Spiezia[c], Elena Campello[c], Kryssia Rodriguez-Castro[a], Alberto Ferrarese[a], Fabio Farinati[b], Patrizia Burra[a], Paolo Simioni[c]

Digestive and Liver Disease 49 (2017) 440–445

Background: Cirrhotic patients with hepatocellular carcinoma (HCC) exhibit hypercoagulability.
Aim: We investigated whether thromboelastometry can detect hypercoagulability in these patients and the association with portal vein thrombosis (PVT).
Methods: At baseline, cirrhotic patients with and without HCC underwent thromboelastometry. PVT onset was recorded over a 12-month follow-up period.
Results: Seventy-six patients (41 with and 35 without HCC) were included. Vital tumor volume (VTV) was >5 cm^3 in 18 patients. Fibrinogen was higher in HCC patients with VTV > 5 cm^3 as compared to those with VTV ≤ 5 cm^3 and those without HCC. Mean platelet count was significantly increased in HCC patients compared with non-HCC. At baseline thromboelastometry, HCC patients showed shorter CTF and higher MCF than non-HCC. PVT incidence was 24,4% and 11.4% in patients with (10/41) and without (4/35) HCC, respectively. Among HCC, 50% of PVT occurred in Child A patients. In HCC, FIBTEM MCF>25 mm was associated with a 5-fold increased PVT risk [RR: 4.8 (2–11.3); p = 0.0001]. Cox multivariate analysis confirmed HCC and increased MCF (FIBTEM) to be independently associated with increased PVT risk.
Conclusions: Hypercoagulability in HCC which can be detected by thromboelastometry is associated with increased risk of PVT even in Child A patients. The clinical implication of these findings deserves further investigation.

Point-of-care thromboelastography/ thromboelastometry-based coagulation management in cardiac surgery: a meta-analysis of 8332 patients

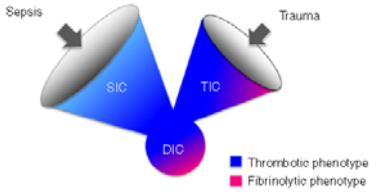
JOURNAL OF SURGICAL RESEARCH • 15 JUNE 2016 (203) 424–433



Defining trauma-induced coagulopathy with respect to future implications for patient management: Communication from the SSC of the ISTH

J Thromb Haemost. 2020;18:740–747

Received: 26 August 2019 | Accepted: 25 November 2019



Redefining postinjury fibrinolysis phenotypes using two viscoelastic assays

Gregory R. Stettler, MD, Ernest E. Moore, MD, Hunter B. Moore, MD, PhD, Geoffrey R. Nunns, MD, Christopher C. Silliman, MD, PhD, Anirban Banerjee, PhD, Angela Sauaia, MD, PhD

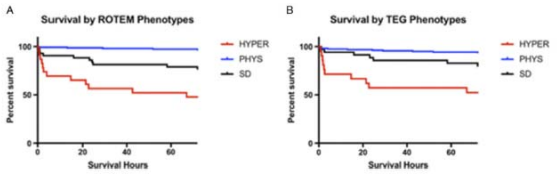


Figure 3.
Kaplan-Meier cruves for survaival in the first 72 hours based on fibrinolysis phenotype by (*A*) ROTEM and (*B*) TEG. Hyperfibrinolysis (HYPER) shows early mortality, while the shutdown fibrinolysis (SD) phenotype has a more delayed mortality. The physiologic fibrinolysis group (PHYS) seems to have a protective effect on both ROTEM and TEG. Log-rank $p < 0.0001$, Wilcoxon $p < 0.0001$ for ROTEM and TEG comparisons.

Evaluation of coagulation status using viscoelastic testing in intensive care patients with coronavirus disease 2019 (COVID-19): An observational point prevalence cohort study

Luke Wallace Collett, MBBS, FCICM [a,b]
Samuel Gluck, BA, MA, MB, BChir, MRCoA (UK) [a,b,*]
Richard Michael Strickland, MBBS, FACEM, JFICM [a,b]
Benjamin John Reddi, MB ChB, FCICM [a,b]

Coagulation profile		Outside range, n (%)	Median [IQR]	Normal range
EXTEM	A10 (mm)	5/6 > NR (83)	70 [68.25 to 74.75]	43–63 mm
	CFT (s)	2/6 <NR (33)	48.5 [41 to 60.5]	46–149 s
	MCF (mm)	5/6 > NR (83)	74.5 [72.5 to 79.5]	55–72 mm
	ML (%)		1.5 [1 to 4.25]	0–15%
FIBTEM	A10 (mm)	6/6 > NR (100)	30.5 [28.25 to 40.25]	6–21 mm
	MCF (mm)	6/6 > NR (100)	38 [30.5 to 45.5]	6–21 mm
	ML (%)		0 [0 to 0]	0–15%
INTEM	A10 (mm)	5/6 > NR (83)	70.5 [66.25 to 71]	43–62 mm
	CFT (secs)	5/6 < NR (83)	39.5 [34.75 to 51]	62–130 s
	MCF (mm)	5/6 > NR (83)	75.5 [72.75 to 77.5]	51–69 mm
	ML (%)		2.5 [0.5 to 4.75]	0–15%
D-dimer (mg/L)			6.1 [2.585 to 9.66]	0–0.59 mg/L
PT (s)			14.7 [14.075 to 14.925]	12–16 s
INR			1.1 [1.025 to 1.1]	0.9–1.2
aPTT (s)				24–38 s
Fibrinogen (g/L)				1.5–4 g/L
Platelets x 10^9/L				150–450 x 10^9/L
ATIII (%)				80–125%
PrC (%)			113 [100.5 to 122.5]	65–130%
PrS (%)			122 [108 to 143.5]	65–155%
Lupus anticoagulant (dRVVT) ratio (secs)	5		6.1 [2.585 to 9.66]	31–51 s

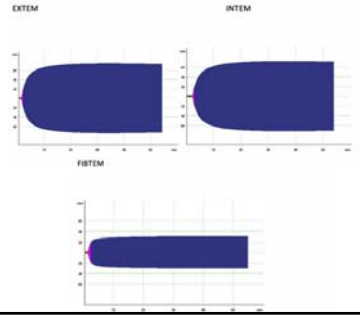
D-dimer Fibrinojen

Diğerleri NORMAL

A10 maximum clot amplitude at 10 min; aPTT activated partial thromboplastin time; ATIII antithrombin III; CFT clot formation time; dRVVT Dilute Russell's viper venom time; INR international normalised ratio; MCF maximum clot firmness; ML lysis index; PrC protein C; PrS protein S; PT prothrombin time; IQR interquartile range.

Evaluation of coagulation status using viscoelastic testing in intensive care patients with coronavirus disease 2019 (COVID-19): An observational point prevalence cohort study

Luke Wallace Collett, MBBS, FCICM [a,b]
Samuel Gluck, BA, MA, MB, BChir, MRCoA (UK) [a,b,*]
Richard Michael Strickland, MBBS, FACEM, JFICM [a,b]
Benjamin John Reddi, MB ChB, FCICM [a,b]



Evaluation of coagulation function by rotation thromboelastometry in critically ill patients with severe COVID-19 pneumonia

Vittorio Pavoni[1] · Lara Gianesello[2] · Maddalena Pazzi[1] · Caterina Stera[1] · Tommaso Meconi[1] · Francesca Covani Frigieri[1]

Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02130-7

Table 3 ROTEM parameters at T0, T5 and T10

	Reference	T0 (n = 40)	T5 (n = 40)	T10 (n = 33)	p value
INTEM					
CT, s	100–240	174.6 ± 26.2	181 ± 20	166 ± 8.1	0.383
CFT, s	30–110	38.8 ± 12.1	24.3 ± 18.6	37 ± 3.1	0.405
A5, mm	38–57	61.4 ± 9.5	65.3 ± 2.5	63.5 ± 3.7	0.709
A10, mm	44–66	70 ± 7.6	75.6 ± 2	70.3 ± 3.3	0.187
MCF, mm	50–72	74.5 ± 6.9	75.7 ± 2.1	79.5 ± 13.3	0.189
EXTEM					
CT, s	38–79	78.3 ± 17.2	78.7 ± 14	64.5 ± 5.8	0.229
CFT, s	34–159	41.6 ± 11.4	37.6 ± 3.2	36.3 ± 5.3	0.434
A5, mm	34–55	63.2 ± 8.5	67.3 ± 3.2	63.8 ± 5	0.766
A10, mm	43–65	71.4 ± 7.5	74 ± 2	71 ± 2	0.567
MCF, mm	50–72	76.6 ± 6.4	77.3 ± 0.6	73.5 ± 3.5	0.471
ML % 60		9.4 ± 6.6	5.2 ± 3.5	5 ± 1.2	0.028*
FIBTEM					
MCF, mm	9–25	35.9 ± 5.9	32.3 ± 8.3	23 ± 3.3	0.017*

*p value < 0.05 between T0 and T10

Fibrinolysis Shutdown Correlation with Thromboembolic Events in Severe COVID-19 Infection

Franklin L Wright, MD, FACS, Thomas O Vogler, PhD, Ernest E Moore, MD, FACS, Hunter B Moore, MD, PhD, Max V Wohlauer, MD, Shane Urban, BSN, RN, Trevor L Nydam, MD, FACS, Peter K Moore, MD, Robert C McIntyre Jr, MD, FACS

Table 2. Coagulation Parameters

Conventional coagulation measurement	Median (IQR)	Reference range
Platelet count, 10^9/L	232 (186–298)	150–400
Prothrombin time, s		12–14.5
Activated partial thro		22.6–34.1
Fibrinogen, mg/dL		150–400
D-dimer, ng/mL fibrinogen equivalent	1,840 (935–4,085)	< 500
Viscoelastic index		
R-time, min	5.8 (4.8–8.6)	2–8
Angle, degrees	71 (66–74)	55–78
Maximum amplitude, mm	73 (67–77)	50–70
Clot lysis at 30 min, %	0 (0–0.4)	0.8–3

IQR, interquartile range.

D-dimer Fibrinojen

Diğerleri NORMAL

Fibrinolysis Shutdown Correlation with Thromboembolic Events in Severe COVID-19 Infection

Franklin L Wright, MD, FACS, Thomas O Vogler, PhD, Ernest E Moore, MD, FACS, Hunter B Moore, MD, PhD, Max V Wohlauer, MD, Shane Urban, BSN, RN, Trevor L Nydam, MD, FACS, Peter K Moore, MD, Robert C McIntyre Jr, MD, FACS

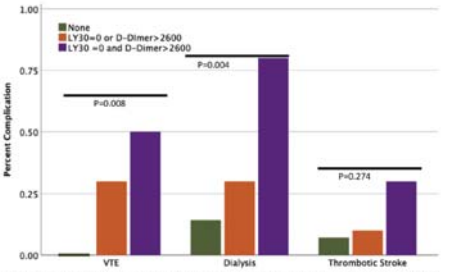
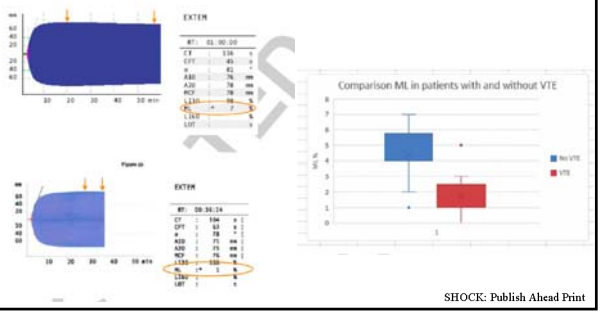


Figure 4. Combination score predicts venous thromboembolic event (VTE) and dialysis risk. LY30, clot lysis at 30 minutes.

Fibrinolysis Shutdown and Thrombosis in a COVID-19 ICU

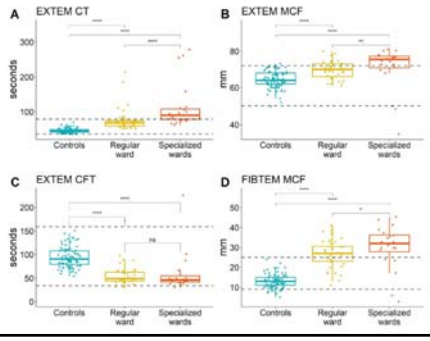
Authors: Christina Creel-Bulos [1], Sara C. Auld[2],Mark Caridi-Scheible [1], Nicholas Barker[3], Sarah Friend[4], Manila Gaddh [4], Christine L. Kempton[2], Cheryl Maier[4], Fadi Nahab[3], Roman Sniecinski[3]



SHOCK: Publish Ahead Print

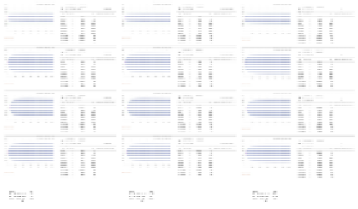
Rotational Thromboelastometry predicts care level in COVID-19

Lou M. Almskog, MD [1 2]; Agneta Wikman, MD, PhD [3]; Jonas Svensson, MD [4]; Michael Wanecek, MD, PhD [1 5]; Matteo Bottai, PhD [6]; Jan van der Linden, MD, PhD [2 7]; Anna Ågren, MD, PhD [8 9].

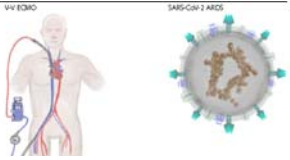


COVID ve ROTEM

- Hızlandırılmış pıhtı oluşumu
- Artan pıhtı gücü
- Hipofibrinoliz / fibrinoliz shut down



ECMO vs COVID

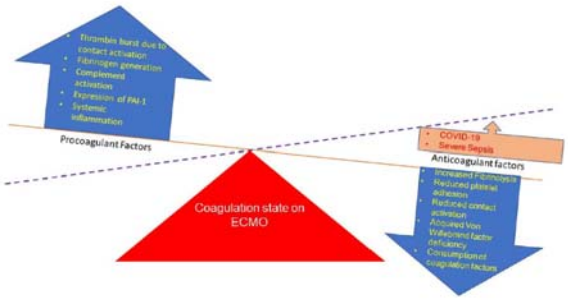


Coagulation and anticoagulation		
Platelet activation	↑	?
Platelet aggregation	↓	?
Platelet activation factor	↑	?
Heparin-induced thrombocytopenia	↑	?
Von Willebrand factor	↓	?
D-dimer	↑	↑↑
Fibrin degradation products		↑↑
Activated partial thromboplastin time	↑	~
Prothrombin time		~
Thrombospondin	↓	?
Fibronectin	↓	?
Thrombin	↑	?
Fibrinogen	Initial ↓	↑
High molecular weight kininogen	↑	?
Prekallikrein	↓	?
Kallikrein	↑	?

ASAIO Journal 2020

Thrombosis and Coagulopathy in COVID-19 Patients Requiring Extracorporeal Membrane Oxygenation

Hakeem Yusuf,*† Vasileios Zochios,*† and Daniel Brodie‡



Extracorporeal membrane oxygenation for COVID-19-associated severe acute respiratory distress syndrome and risk of thrombosis

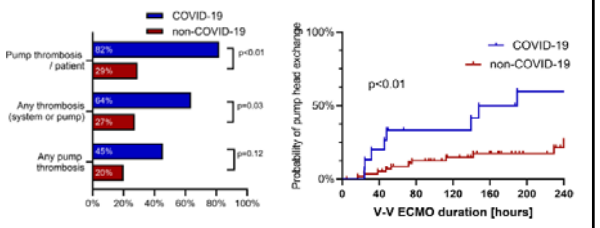
Christophe Beyls*, Pierre Huette, Osama Abou-Arab, Pascal Berna and Yazine Mahjoub

Anticoagulation therapy before ECMO	6 (50)
Thrombotic complications	4 (33)
Cannula thrombosis	2 (17)
Oxygenator thrombosis	1 (8)
Massive PE	1 (8)
Death related to thrombotic complication	2 (17)
Outcome	
Still on ECMO	8 (66)
ECMOvv converted to ECMOva	0
Weaned from ECMO and still in hospital	2 (16)
Weaned from MV	1 (8)
Discharge from ICU	0
Discharge from hospital	0

Thrombotic circuit complications during venovenous extracorporeal membrane oxygenation in COVID-19

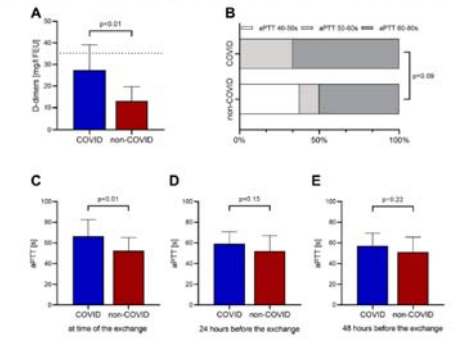
Xavier Berntgen[1,2] · Viviane Zotzmann[1,2] · Christoph Benk[3] · Jonathan Rilinger[1,2] · Katrin Steiner[1,3,4] · Alexander Asmussen[1,2] · Christoph Bode[1,2] · Tobias Wengenmayer[1,2] · Sven Maier[3] · David L. Staudacher[1,2]

Journal of Thrombosis and Thrombolysis
https://doi.org/10.1007/s11239-020-02217-4



Thrombotic circuit complications during venovenous extracorporeal membrane oxygenation in COVID-19

Xavier Berntgen[1,2] · Viviane Zotzmann[1,2] · Christoph Benk[3] · Jonathan Rilinger[1,2] · Katrin Steiner[1,3,4] · Alexander Asmussen[1,2] · Christoph Bode[1,2] · Tobias Wengenmayer[1,2] · Sven Maier[3] · David L. Staudacher[1,2]



SONUÇ

- COVID pıhtılaşmaya yatkınlık yaratıyor.
- TF ekspresyonu ve hipofibrinoliz en önemli mekanizma
- ECMO+COVID hastalarında heparinizasyona rağmen tromboz ↑
- ROTEM-COVID-ECMO kombinasyonunda çalışmalara ihtiyaç var