GÖĞÜS KALP DAMAR ANESTEZİ VE YOĞUN BAKIM DERNEĞİ

27. Ulusal Kongresi

24 - 25 Eylül 2021 Wyndham Grand İzmir Özdilek

ECMO uygulanan COVİD 19 olgularında koagulasyon yönetimi

Sema Turan

ECMO, COVID-19 ve Koagülasyon

Prof.Dr.Sema TURAN
Sağlık Bilimleri Üniversitesi
Ankara Şehir Hastanesi

- COVID 19 ve ECMO
- COVID 19’da Koagülasyon
- ECMO’da Koagülasyon
- ECMO’lu COVID 19 hastasında koagülasyonun yönetimi

DÜNYADA DURUM

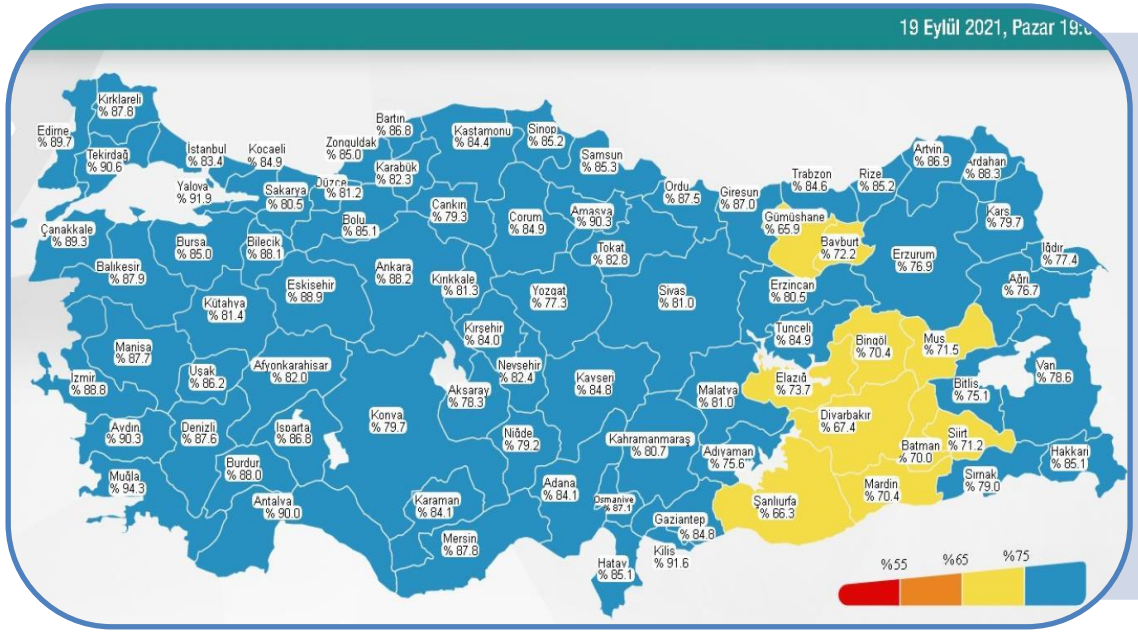
Coronavirus Cases:

227,471,677

Deaths:

4,677,080

ÜLKEMİZDE DURUM



Coronavirus Cases:

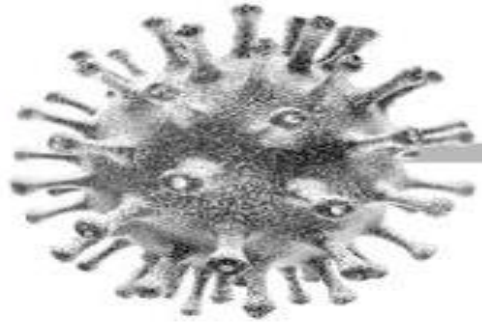
6.847.229

Deaths:

61.574

Coronaviruslar

Uzun zamandır var olan büyük bir virus ailesi
Kışın en sık soğuk algınlığı etkeni
Biyoçeşitliliği çok olan bir virus



2019-nCOV SALGIN

31 Aralık 2019

Semptomlar

- Kuluçka dönemi: 2-14 gün
- Ateş
- Öksürük
- Solunum sıkıntısı
- Pnömoni
- Bozulmuş karaciğer ve böbrek fonksiyonları
- Böbrek yetmezliği

Yeni Coronavirus (2019-nCoV)

31 Aralık 2019'da Çin'in Hubei eyaletinin Wuhan şehrinde pnömoni vakaları olarak ortaya çıktı ve 7 Ocak 2020'de tanımlandı

MERS (Orta Doğu Solunum Sendromu)

2012-Suudi Arabistan, 27 ülkeye yayılım,
2494 konfirme vaka, 858 ölüm

SARS (Ağır Akut Solunum Sendromu)

2002-Çin, 30 ülkeye yayılım,

ORIGINAL ARTICLE

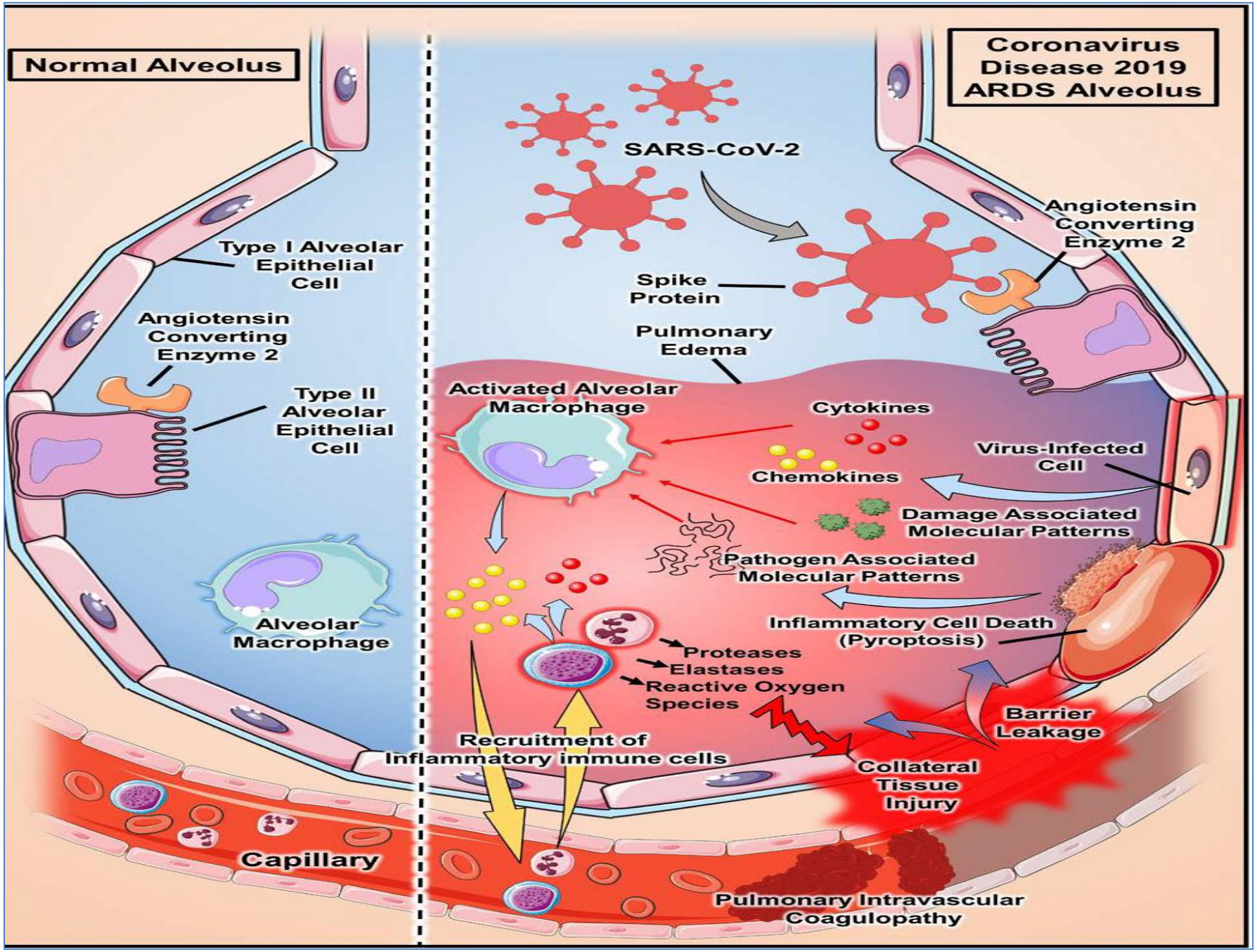
Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan

A Retrospective Observational Study

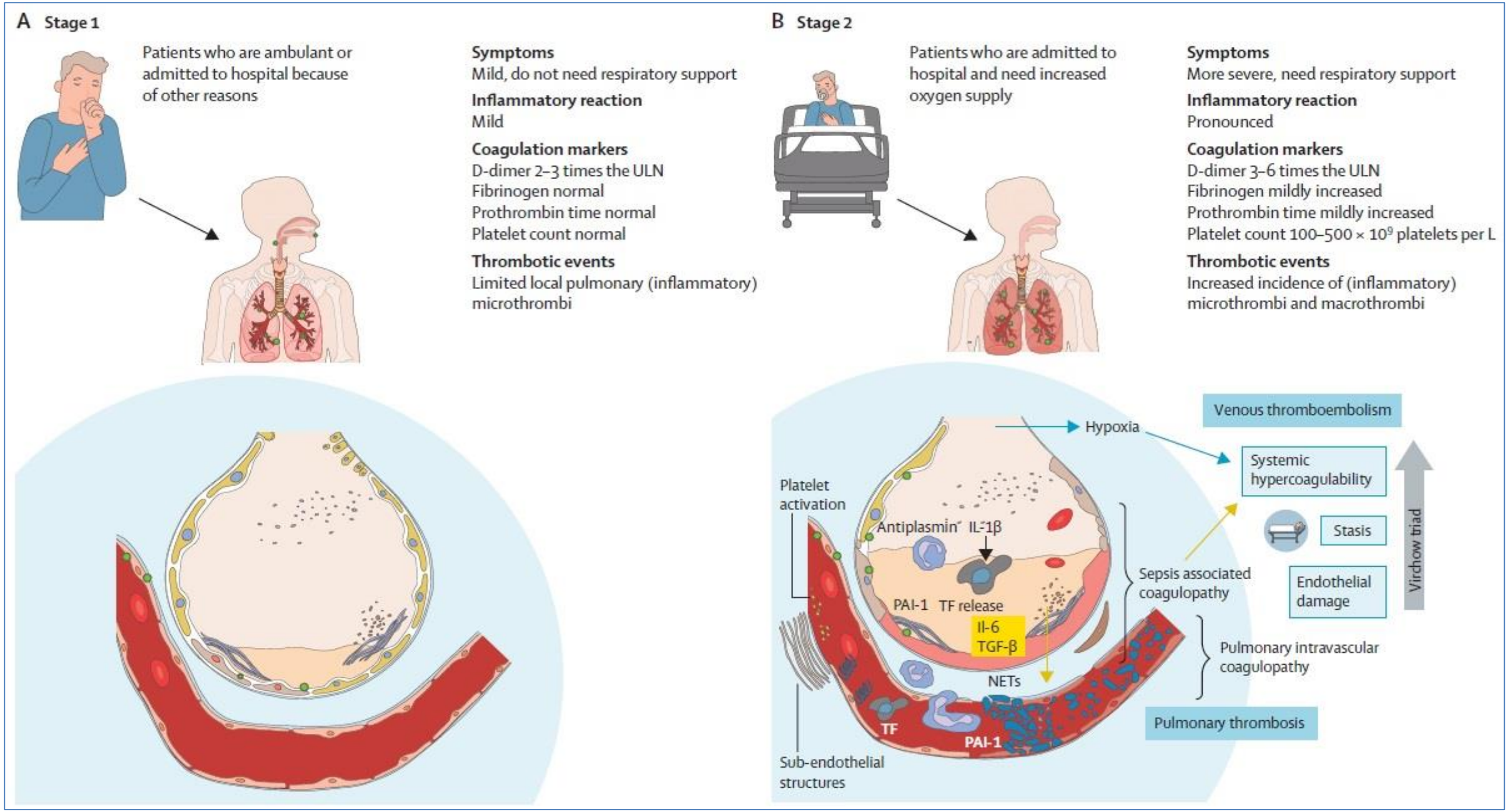
Yingzhen Du[1*], Lei Tu[2*], Pingjun Zhu[1*], Mi Mu[1*], Runsheng Wang[1], Pengcheng Yang[3,4], Xi Wang[5], Chao Hu[6], Rongyu Ping[6], Peng Hu[6], Tianzhi Li[6], Feng Cao[6], Christopher Chang[7,8‡], Qinyong Hu[3,4‡], Yang Jin[9‡], and Guogang Xu[6‡]

Table 5. Complications and Management of Patients with COVID-19

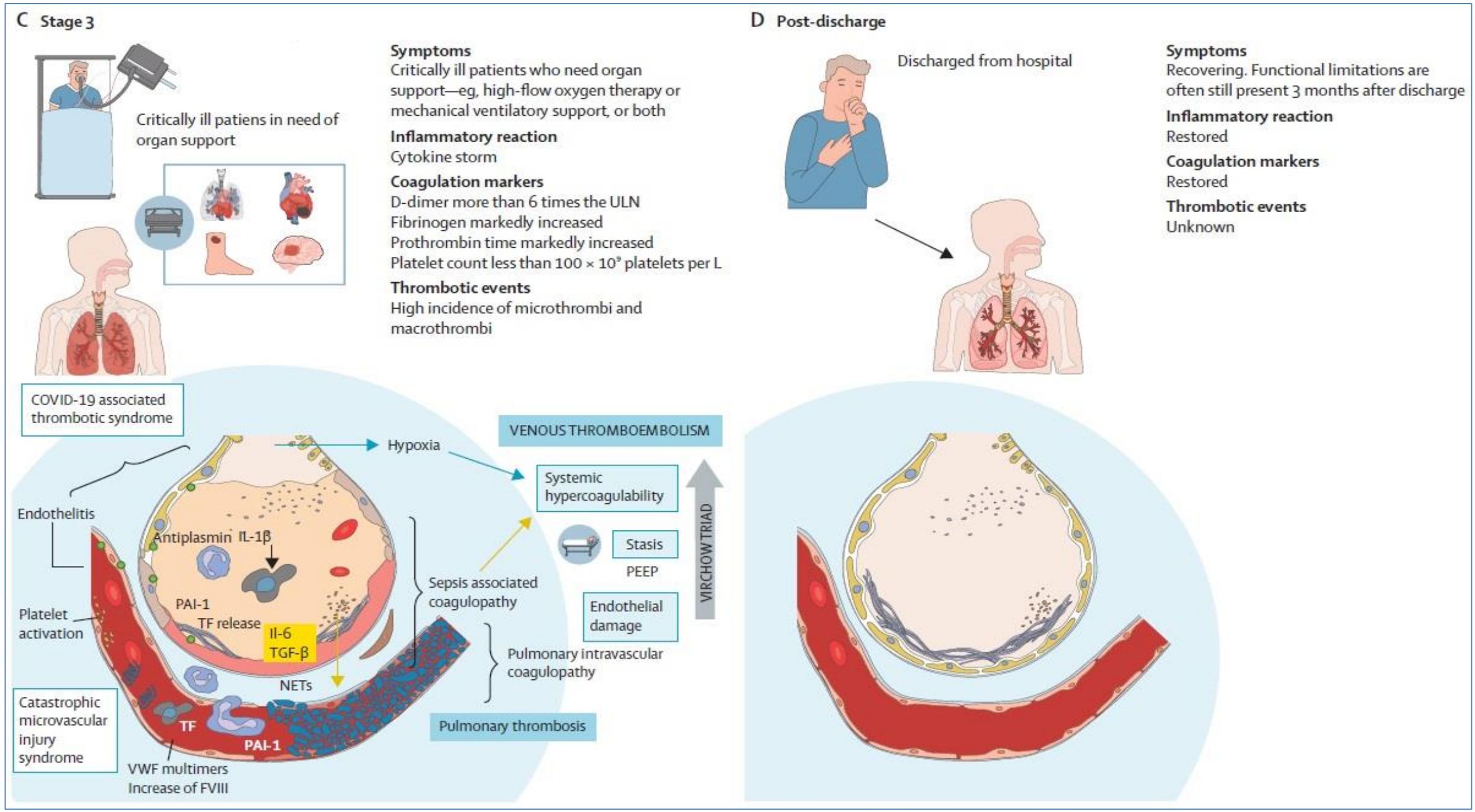
	n (%) (*n* = 85)
Complications	
Respiratory failure	80 (94.1)
Shock	69 (81.2)
ARDS	63 (74.1)
Arrhythmia	51 (60)
Acute cardiac injury	38 (44.7)
Acute liver injury	30 (35.3)
Sepsis	28 (32.9)



Anesthesiology 2021; 134:270–82. DOI: 10.1097/ALN.0000000000003571



COVID-19-associated coagulopathy and antithrombotic agents—lessons after 1 year Leentjens, Jenneke et al. The Lancet Haematology, Volume 8, Issue 7, e524 - e533



COVID-19-associated coagulopathy and antithrombotic agents—lessons after 1 year Leentjens, Jenneke et al. The Lancet Haematology, Volume 8, Issue 7, e524 - e533

Tzotzos et al. Critical Care (2020) 24:516
https://doi.org/10.1186/s13054-020-03240-7

Critical Care

RESEARCH LETTER Open Access

Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey

Susan J. Tzotzos[1*], Bernhard Fischer[1], Hendrik Fischer[1] and Markus Zeitlinger[2]

Table 2 Incidence of ARDS, IMV treatment, and outcomes in COVID-19 patients admitted to an ICU

Study author, online publication date[a]	Location	ICU patients with ARDS	ICU patients who received IMV	Mortality ICU patients	Mortality ARDS patients	Mortality IMV patients	Prevalence of ARDS in non-survivors
Dreher M, 17/4	Aachen, Germany	24/24 (100)	24/24 (100)	3/24 (13)	3/24 (13)	3/24 (13)	3/7 (43)
Yao Q, 24/4	Huanggang, China	17/17 (100)	10/17 (59)	12/17 (71)	12/45 (27)	10/10 (100)	12/12 (100)
Hong K, 11/5	Daegu, South Korea	13/13 (100)	11/13 (85)	4/13 (31)	4/18 (22)	NA	4/5 (80)
Xu X,19/2	Zhejiang, China	1/1 (100)	1/1 (100)	0/1 (0)	0/1 (0)	0/1 (0)	NA
Wu C, 13/3	Wuhan, China	NA	6/53 (11)	NA	44/84 (52)	6/6 (100)	44/44 (100)
Zhou F, 11/3	Wuhan, China	NA	NA	39/50 (78)	50/59 (85)	31/32 (97)	50/54 (93)
Zheng Y, 10/4	Chengdu, China	15/32 (47)	NA	3/32 (9)	3/15 (20)	NA	3/3 (100)
Suleyman G, 1/6	Detroit, Michigan, USA	104/141 (74)	114/141 (81)	57/141 (40)	NA	52/114 (46)	NA
Huang C, 24/1	Wuhan, China	11/13 (85)	4/13 (31)	5/13 (38)	NA	NA	NA
Wang D, 7/2	Wuhan, China	22/36 (61)	21/36 (58)	6/36 (17)	NA	NA	NA
Yang L, 26/5	Yichang, China	21/29 (72)	16/29 (55)	14/29 (48)	NA	NA	NA
Chen T, 26/3	Wuhan, China	NA	NA	NA	113/196 (58)	17/17 (100)	113/113 (100)
Aggarwal S, 26/4	Des Moines, Iowa, USA	NA	5/8 (63)	3/8 (38)	NA	NA	NA
Inciardi R, 8/5	Brescia, Italy	NA	NA	NA	17/19 (89)	NA	17/26 (65)
Chen N, 30/1	Wuhan, China	NA	NA	NA	11/17 (65)	NA	11/11 (100)
Ciceri F, 12/6	Milan, Italy	NA	NA	NA	65/245 (27)	NA	65/82 (79)
Yu T, 27/4	Dongguan, China	NA	NA	NA	NA	NA	NA
Total (weighted average)		228/306 (75)	212/335 (63)	146/363 (40)	322/722 (45)	119/203 (59)	322/357 (90)

Data are presented as *n*/*N*(%)

Abbreviations: *ARDS* acute respiratory distress syndrome, *COVID-19* coronavirus disease 2019, *ICU* intensive care unit, *IMV* invasive mechanical ventilation, *NA* not available: insufficient data for calculation

[a]For study reference see Table 1

General schema for respiratory support in patients with COVID-19

Deterioration

Recovery

Low flow nasal cannula
- Typically set at 1-6 liters/minute.

High flow nasal cannula
- Titrate FiO2 based on patient's saturation. If FiO2 requirement escalating (e.g. over ~80%) consider awake pronation or CPAP trial.
- Consider limiting flow rate below ~40 L/min to reduce aerosolization.
- N95 mask & aerosol precautions.

CPAP
- Titrate CPAP up as tolerated (in more severe hypoxemia might target ~15-18 cm)
- Viral filter.
- N95 mask & aerosol precautions.
- (Helmet interface likely ideal if available).

Awake pronation plus {High Flow Nasal Cannula or CPAP}
- If tolerated, awake patient may lie in a prone position (ideally for 12-18 hr/day).
- Limited to cooperative patients. *May be useful if access to ventilator is limited.*

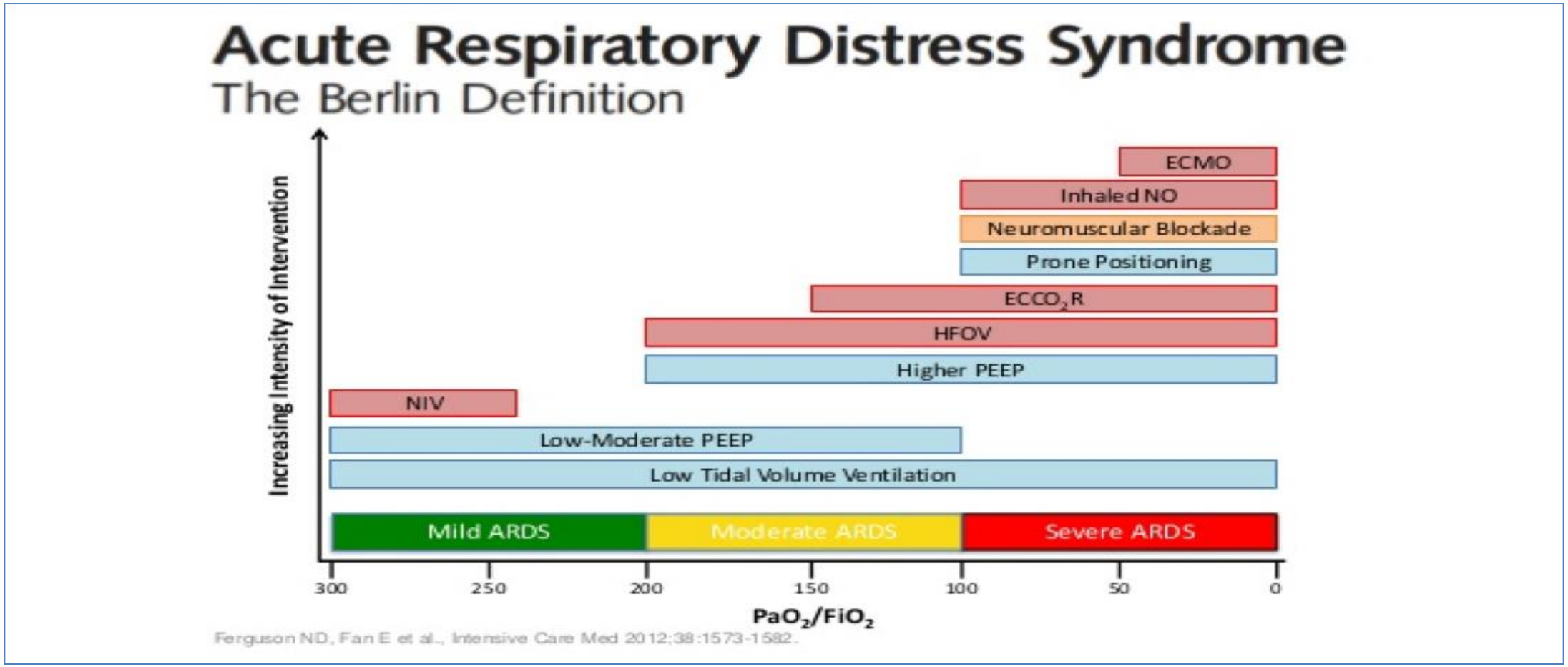
Invasive mechanical ventilation
- Target tidal volumes of ~6 cc/kg.
- Permissive hypercapnia may be useful to allow for lung-protective settings.
- May use conventional lung-protective ventilation strategies or APRV.

Prone positioning
- Consider for severe hypoxemia (e.g. PaO2/FiO2 << 150) that doesn't respond to ~12-24 hours of invasive ventilation with high mean airway pressure (e.g. high PEEP or APRV).

VV-ECMO
- Indications remain unclear.
- Early discussion with ECMO center or team may be advisable.

The optimal strategy for respiratory support in COVID-19 remains unknown. Patients with more complex respiratory disease (e.g. COPD plus COVID-19) might benefit from BiPAP. Choice of CPAP vs. HFNC may vary depending to resources and patient preference. COVID appears to cause progressive micro-atelectasis, which responds well to CPAP.

ARDS'de ECMO


Acute Respiratory Distress Syndrome
The Berlin Definition
Increasing Intensity of Intervention
ECMO
Inhaled NO
Neuromuscular Blockade
Prone Positioning
ECCO2R
HFOV
Higher PEEP
NIV
Low-Moderate PEEP
Low Tidal Volume Ventilation
Mild ARDS
Moderate ARDS
Severe ARDS
300
250
200
150
100
50
0
PaO2/FiO2
Ferguson ND, Fan E et al., Intensive Care Med 2012;38:1573-1582.

[Critical Care How I Do It]

CHEST

How I Select Which Patients With ARDS Should Be Treated With Venovenous Extracorporeal Membrane Oxygenation

E. Caroline Bullen, MBBS; Ricardo Teijeiro-Paradis, MD; and Eddy Fan, MD, PhD

Eligibility Criteria:

- Does the patient fulfil oxygenation and/or ventilation criteria?
  - On FiO2 ≥ 80%, PEEP ≥ 10 cmH_2O, VT ≤ 6ml/kg (PBW)
    - PaO2/FiO2 < 50 mmHg for > 3 hours
    - PaO2/FiO2 < 80 mmHg for > 6 hours
    - pH < 7.25, PaCO2 ≥ 60 mmHg with RR 35/min for > 6 H
- Is the underlying disease reversible?
- Has conventional mechanical ventilation been optimized?
  - Lung protective ventilation
  - PEEP optimization
  - Neuromuscular blockade
  - Prone position ventilation

Contraindications:

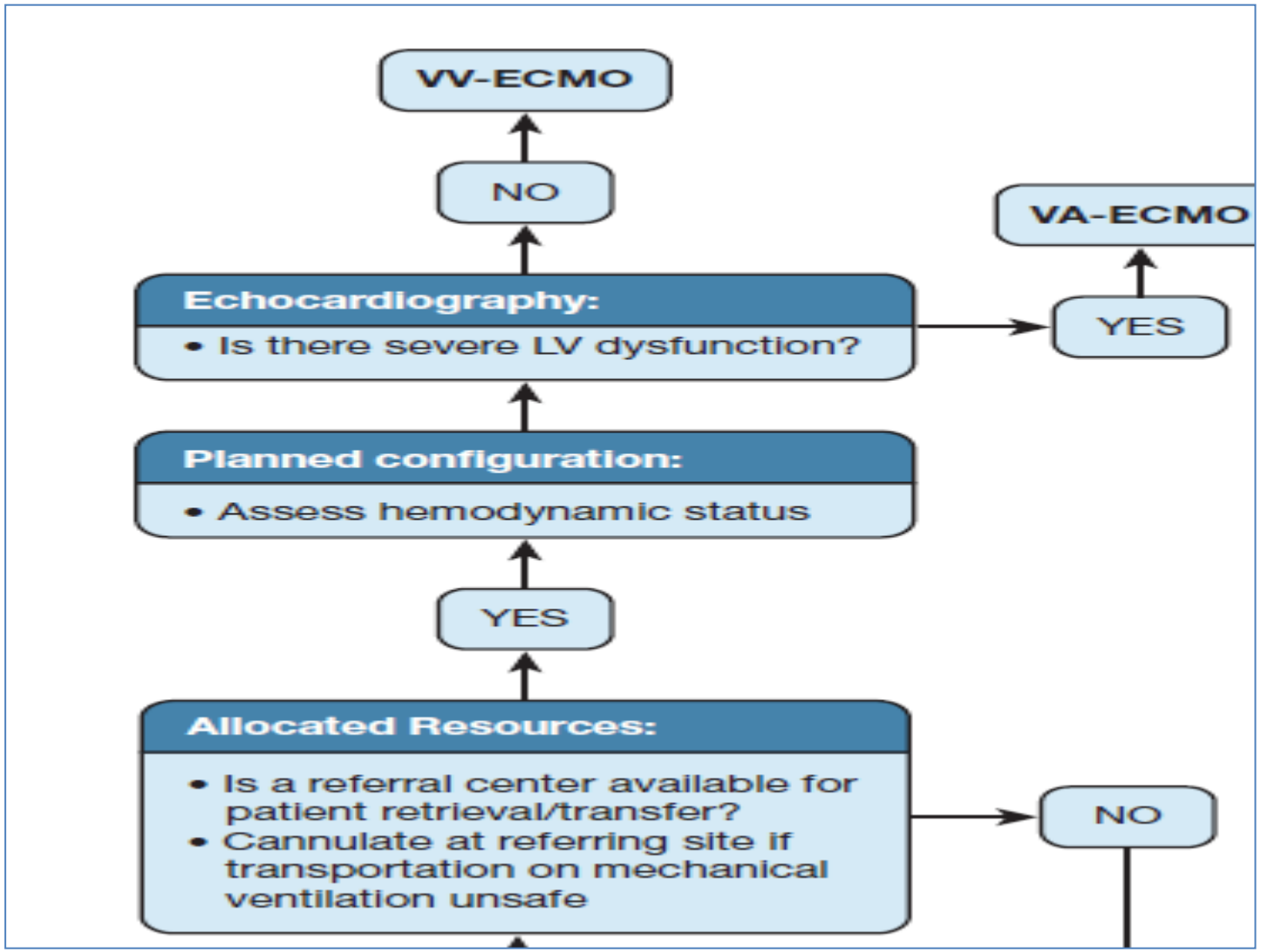
- Has the patient received prolonged injurious mechanical ventilation?
- Is there an unacceptably high risk of hemorrhagic complications?
- Unable to obtain adequate vascular access/cannulation?
- Profound distributive shock with preserved/hyperdynamic LV function?

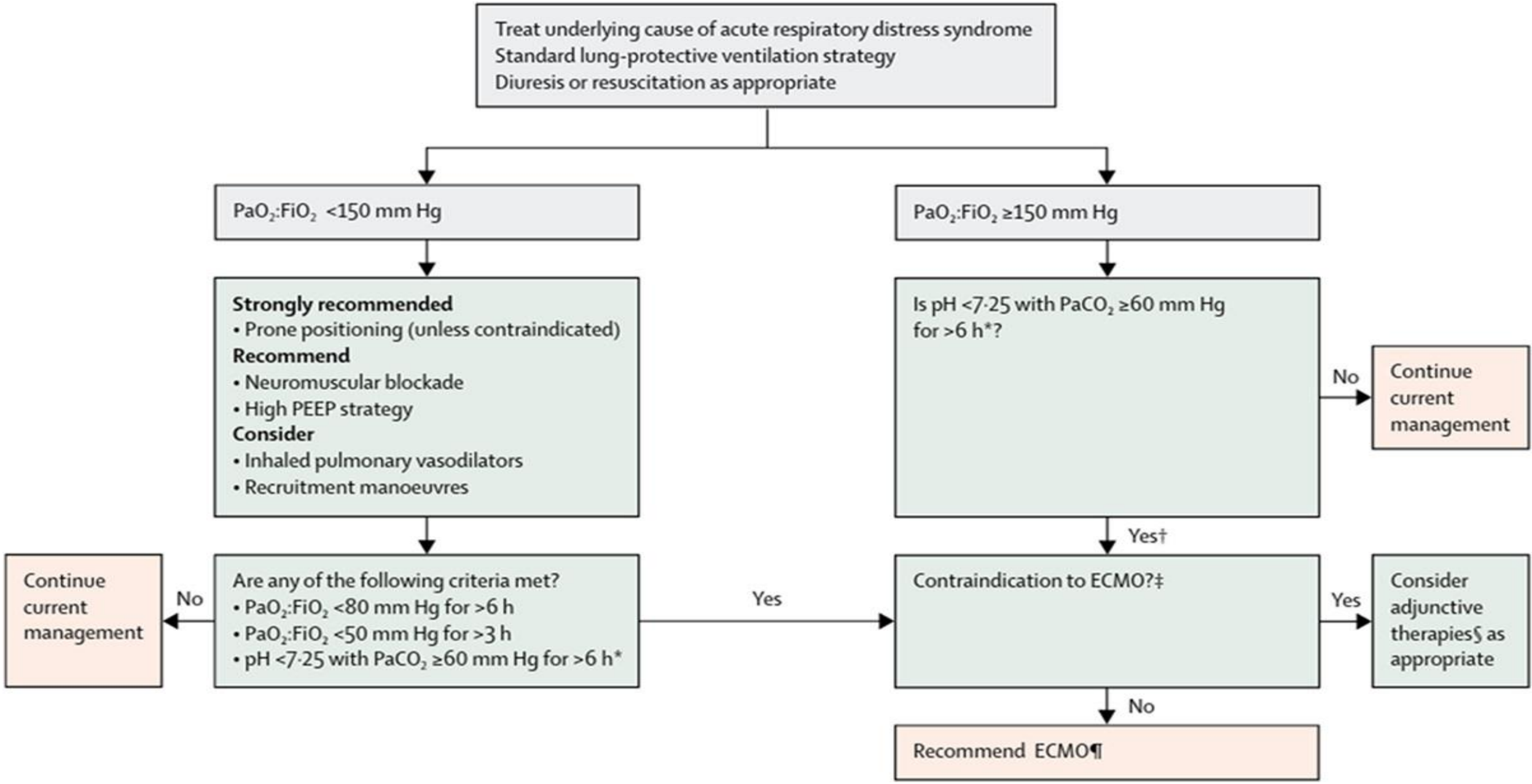
CHEST 2020; 158(3):1036-1045

CHEST

How I Select Which Patients With ARDS Should Be Treated With Venovenous Extracorporeal Membrane Oxygenation

E. Caroline Bullen, MBBS; Ricardo Teijeiro-Paradis, MD; and Eddy Fan, MD, PhD



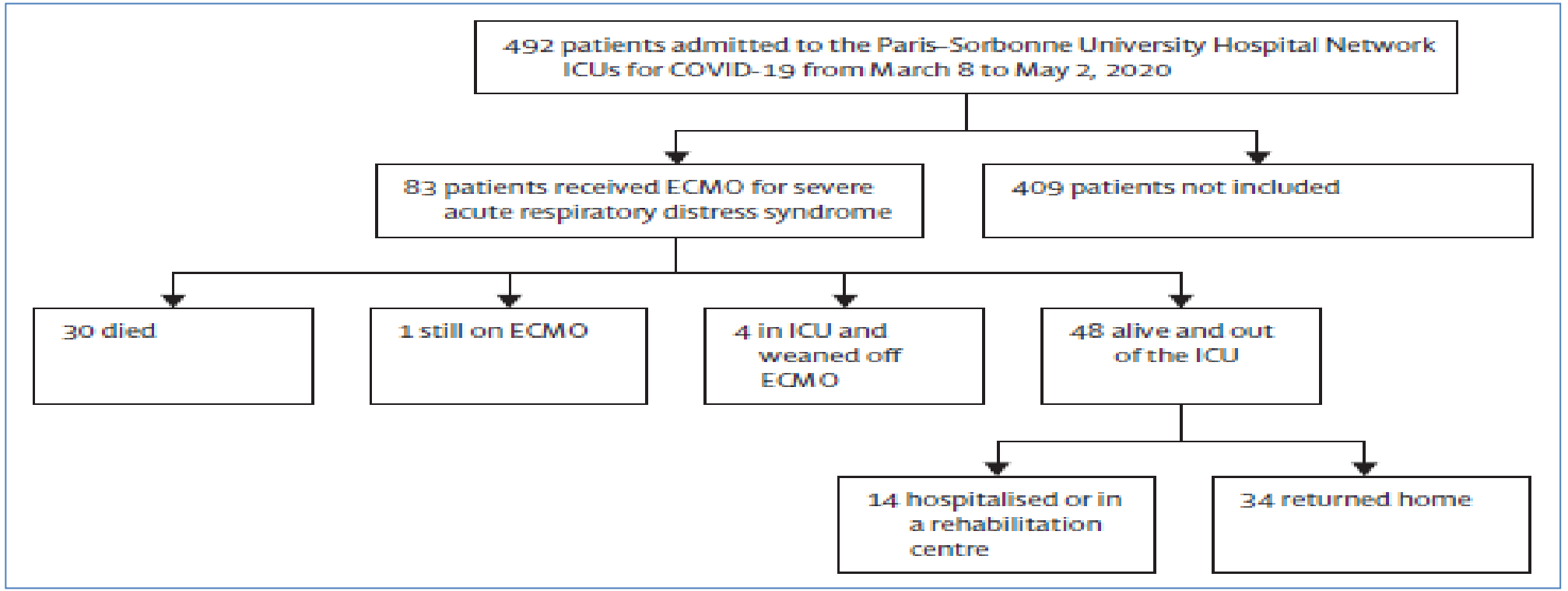

Treat underlying cause of acute respiratory distress syndrome
Standard lung-protective ventilation strategy
Diuresis or resuscitation as appropriate
PaO2:FiO2 <150 mm Hg
PaO2:FiO2 ≥150 mm Hg
Strongly recommended
• Prone positioning (unless contraindicated)
Recommend
• Neuromuscular blockade
• High PEEP strategy
Consider
• Inhaled pulmonary vasodilators
• Recruitment manoeuvres
Is pH <7·25 with PaCO2 ≥60 mm Hg for >6 h*?
No
Continue current management
Yes†
Are any of the following criteria met?
• PaO2:FiO2 <80 mm Hg for >6 h
• PaO2:FiO2 <50 mm Hg for >3 h
• pH <7·25 with PaCO2 ≥60 mm Hg for >6 h*
No
Continue current management
Yes
Contraindication to ECMO?‡
Yes
Consider adjunctive therapies§ as appropriate
No
Recommend ECMO¶

COVID-19 Cases on ECMO in the ELSO Registry

Total COVID-19 Cases	COVID-19 Suspected or Confirmed 9203	COVID-19 Confirmed Cases 9170
Patients who initiated ECMO at least 90 days ago	COVID-19 Confirmed 7605	COVID-19 In-hospital Mortality 48%

Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study

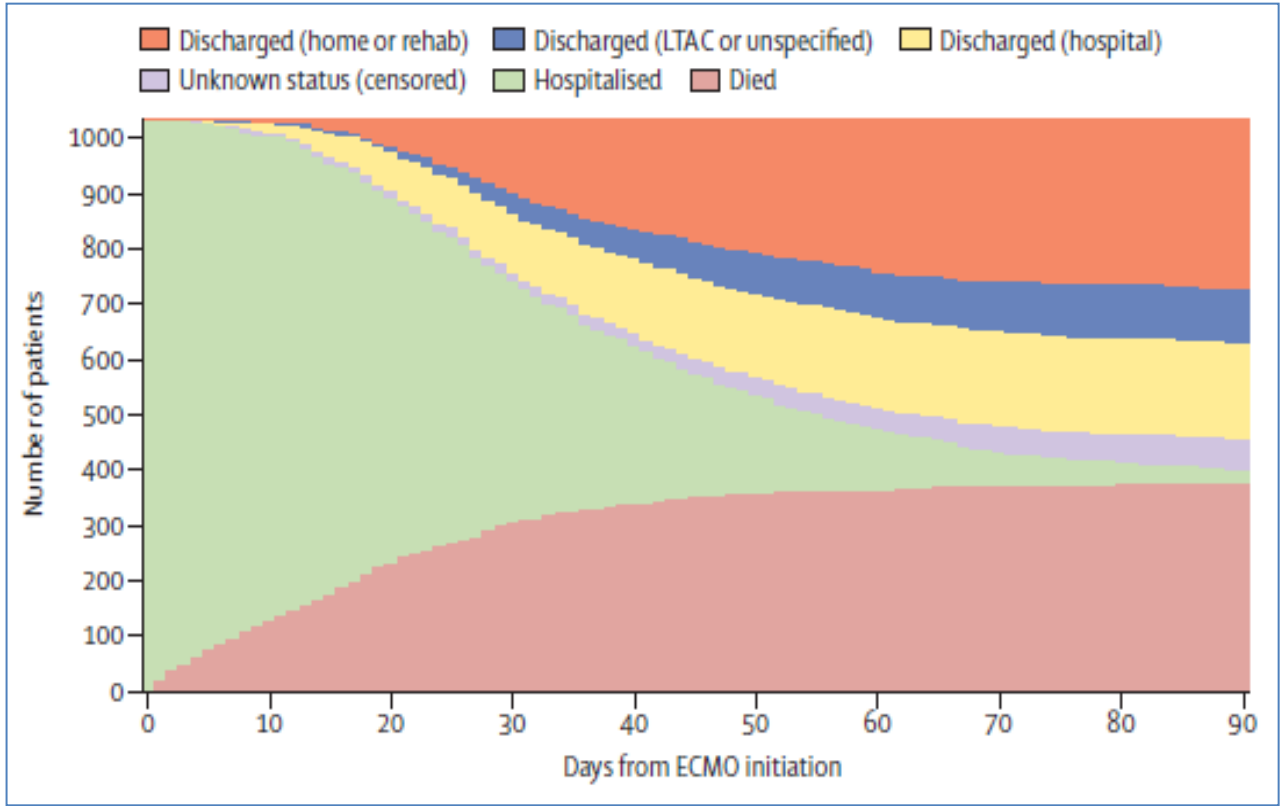
*Matthieu Schmidt, David Hajage, Guillaume Lebreton, Antoine Monsel, Guillaume Voiriot, David Levy, Elodie Baron, Alexandra Beurton, Juliette Chommeloux, Paris Meng, Safaa Nemlaghi, Pierre Bay, Pascal Leprince, Alexandre Demoule, Bertrand Guidet, Jean Michel Constantin, Muriel Fartoukh, Martin Dres, Alain Combes, for the Groupe de Recherche Clinique en REanimation et Soins intensifs du Patient en Insuffisance Respiratoire aiguE (GRC-RESPIRE) Sorbonne Université, and the Paris-Sorbonne ECMO-COVID investigators**



Lancet Respir Med 2020

Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry

Ryan P Barbaro, Graeme MacLaren*, Philip S Boonstra, Theodore J Iwashyna, Arthur S Slutsky, Eddy Fan, Robert H Bartlett, Joseph E Tonna, Robert Hyslop, Jeffrey J Fanning, Peter T Rycus, Steve J Hyer, Marc M Anders, Cara L Agerstrand, Katarzyna Hryniewicz, Rodrigo Diaz, Roberto Lorusso†, Alain Combes†, Daniel Brodie†, for the Extracorporeal Life Support Organization‡*



	Full cohort (n=1035)	ARDS cohort* (n=779)
Patient status at study completion		
Discharged alive to home or acute rehabilitation centre	311 (30%)	262 (34%)
Discharged alive to long-term acute care centre or unspecified location	101 (10%)	79 (10%)
Discharged to another hospital	176 (17%)	97 (12%)
Remain in the hospital (discharged from ICU)	11 (1%)	10 (1%)
Remain in the ICU	56 (5%)	40 (5%)
In-hospital death	380 (37%)	291 (37%)
Tracheostomy†	444 (44%)	353 (47%)
Select complications‡		
Seizure	6 (0·6%)	5 (0·7%)
CNS infarct	7 (0·7%)	5 (0·7%)
CNS haemorrhage	56 (6%)	44 (6%)
Haemolysis	48 (5%)	37 (5%)
Membrane lung failure	82 (8%)	63 (9%)
Pump failure	8 (0·8%)	6 (0·8%)
Circuit change	148 (15%)	99 (13%)

Lancet 2020; 396: 1071–78

Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry

Ryan P Barbaro, Graeme MacLaren*, Philip S Boonstra, Theodore J Iwashyna, Arthur S Slutsky, Eddy Fan, Robert H Bartlett, Joseph E Tonna, Robert Hyslop, Jeffrey J Fanning, Peter T Rycus, Steve J Hyer, Marc M Anders, Cara L Agerstrand, Katarzyna Hryniewicz, Rodrigo Diaz, Roberto Lorusso†, Alain Combes†, Daniel Brodie†, for the Extracorporeal Life Support Organization‡*

	Full cohort (n=1035)		ARDS cohort* (n=779)	
	N	Median (IQR) or n (%)	N	Median (IQR) or n (%)
Non-invasive ventilation				
Non-invasive ventilation before intubation	1032	606 (59%)	776	434 (56%)
BiPAP	1032	185 (18%)	776	119 (15%)
CPAP	1032	140 (14%)	776	80 (10%)
HFNC	1032	357 (35%)	776	285 (37%)
Pre-ECMO intubation (days)	914	4·0 (1·8–6·4)	688	4·3 (2·0–6·5)
Conventional ventilation†	951	942 (99%)	729	721 (99%)
PEEP (cm H_2O)	868	14 (12–16)	661	15 (12–18)
PIP (cm H_2O)	699	33 (30–38)	532	34 (30–38)
FiO_2	888	1·0 (0·90–1·0)	672	1·0 (0·90–1·0)
PaO_2:FiO_2 (mm Hg)	868	72 (59–94)	657	72 (60–93)
$PaCO_2$ (mm Hg)	896	60 (50–74)	678	60 (50–74)
Pre-ECMO support				
Prone positioning	1019	612 (60%)	766	464 (61%)
Neuromuscular blockade	1015	729 (72%)	762	567 (74%)
Inhaled pulmonary vasodilators	1019	293 (29%)	766	242 (32%)
Any vasoactive support	1015	606 (60%)	758	447 (59%)
Norepinephrine	1015	561 (55%)	762	416 (55%)
COVID-19 therapies and immunomodulators				
Any therapy	1035	786 (76%)	779	633 (81%)
Glucocorticoids	1035	420 (41%)	779	331 (42%)
Intravenous immunoglobin	1035	29 (3%)	779	22 (3%)
Anticytokine	1035	289 (28%)	779	261 (34%)
Lopinavir-ritonavir	1035	116 (11%)	779	103 (13%)
JAK inhibition	1035	7 (0·7%)	779	5 (0·6%)
Chloroquine or hydroxychloroquine	1035	538 (52%)	779	443 (57%)
Remdesivir	1035	84 (8%)	779	69 (9%)
Support type				
Respiratory	1035	995 (96%)	779	777 (99·7%)
Cardiac	1035	29 (3%)	779	0
ECPR	1035	11 (1%)	779	2 (0·3%)

Perspective

Extracorporeal membrane oxygenation (ECMO): does it have a role in the treatment of severe COVID-19?

Xiaoyang Hong[a,1], Jing Xiong[b,c,d,e,f,1], Zhichun Feng[a,*], Yuan Shi[b,c,d,e,f,**]

[a] Bayi Children's Hospital, The Seventh Medical Center, PLA General Hospital, Beijing, China
[b] Department of Neonatology, Ministry of Education Key Laboratory of Child Development and Disorders, PR China
[c] National Clinical Research Center for Child Health and Disorders, PR China
[d] China International Science and Technology Cooperation base of Child development and Critical Disorders, PR China
[e] Children's Hospital of Chongqing Medical University, PR China
[f] Chongqing Key Laboratory of Pediatrics, Chongqing, 400014, PR China

Table 2
Current clinical uses of ECMO for COVID-19

Application	Study design	Cases on ECMO (total cases)	Outcomes of ECMO	Reference
Critically ill patients with SARS-CoV-2 pneumonia	Single center, retrospective, study	6 (52)	Five patients died while one patient was still on ECMO at the endpoint	(Yang et al., 2020)
Patients with ARDS caused by SARS-CoV-2	Single center, retrospective study	10 (221)	Two patients were discharged, three patients died, and five patients were still on ECMO at the endpoint	(Guqin et al., 2020)
Critically ill patients with SARS-CoV-2 pneumonia	Single center, retrospective study	4 (138)	NA	(Guan et al., 2020)
Critically ill patients with SARS-CoV-2 pneumonia	Multicenter retrospective study	5 (1099)	NA	(Huang et al., 2020)
Critically ill patients with SARS-CoV-2 pneumonia	Single center prospective study	2 (41)	NA	(Brodie et al., 2019)

ARDS = acute respiratory distress syndrome; COVID-19= coronavirus disease 2019; ECMO = extracorporeal membrane oxygenation; NA = not available; SARS-CoV-2= severe acute respiratory syndrome coronavirus 2.

Cho et al. Critical Care (2020) 24:301
https://doi.org/10.1186/s13054-020-02979-3

Critical Care

REVIEW Open Access

ECMO use in COVID-19: lessons from past respiratory virus outbreaks—a narrative review

Hwa Jin Cho[1,2*†], Silver Heinsar[1†], In Seok Jeong[3], Kiran Shekar[1,4], Gianluigi Li Bassi[1,5], Jae Seung Jung[1,6], Jacky Y. Suen[1] and John F. Fraser[1,4]

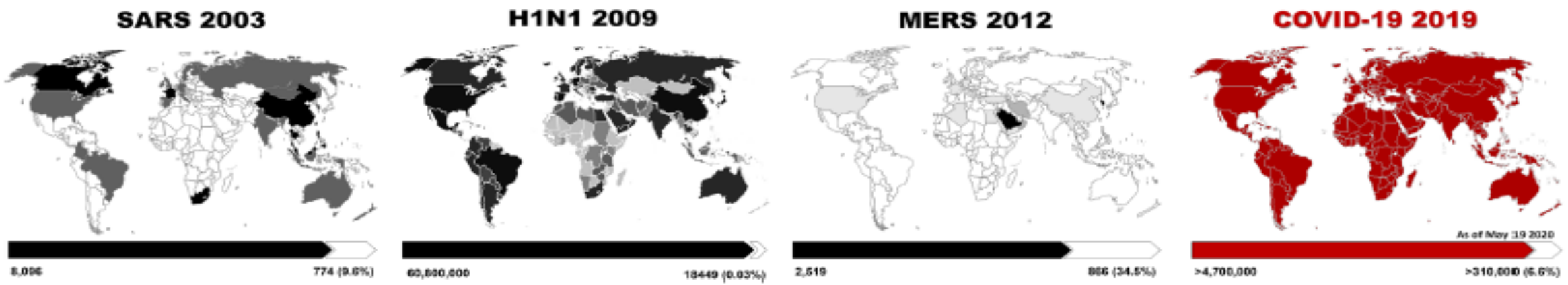


Fig. 1 Geographical distribution in previous viral outbreaks with the name of viral outbreaks and onset year. The number of infected cases (coloured bar) and number of deaths (blank bar) with percentage of death are described under each map. The length of the bars represent the approximate ratio of infected cases to deaths. The geographic distribution in COVID-19 is not expressed in this figure since the numbers and countries are still changing. As of May 19, 2020, total infected numbers of cases are over 4,700,000 and over 310,000 (6.6%) died of COVID-19. *SARS* Severe acute respiratory syndrome; *MERS* Middle East respiratory syndrome; *COVID-19* Coronavirus disease 2019

Table 2 Demographic data, the patient characteristics and ECMO data of 8 multicentre studies with H1N1 outbreak (2009–2010)

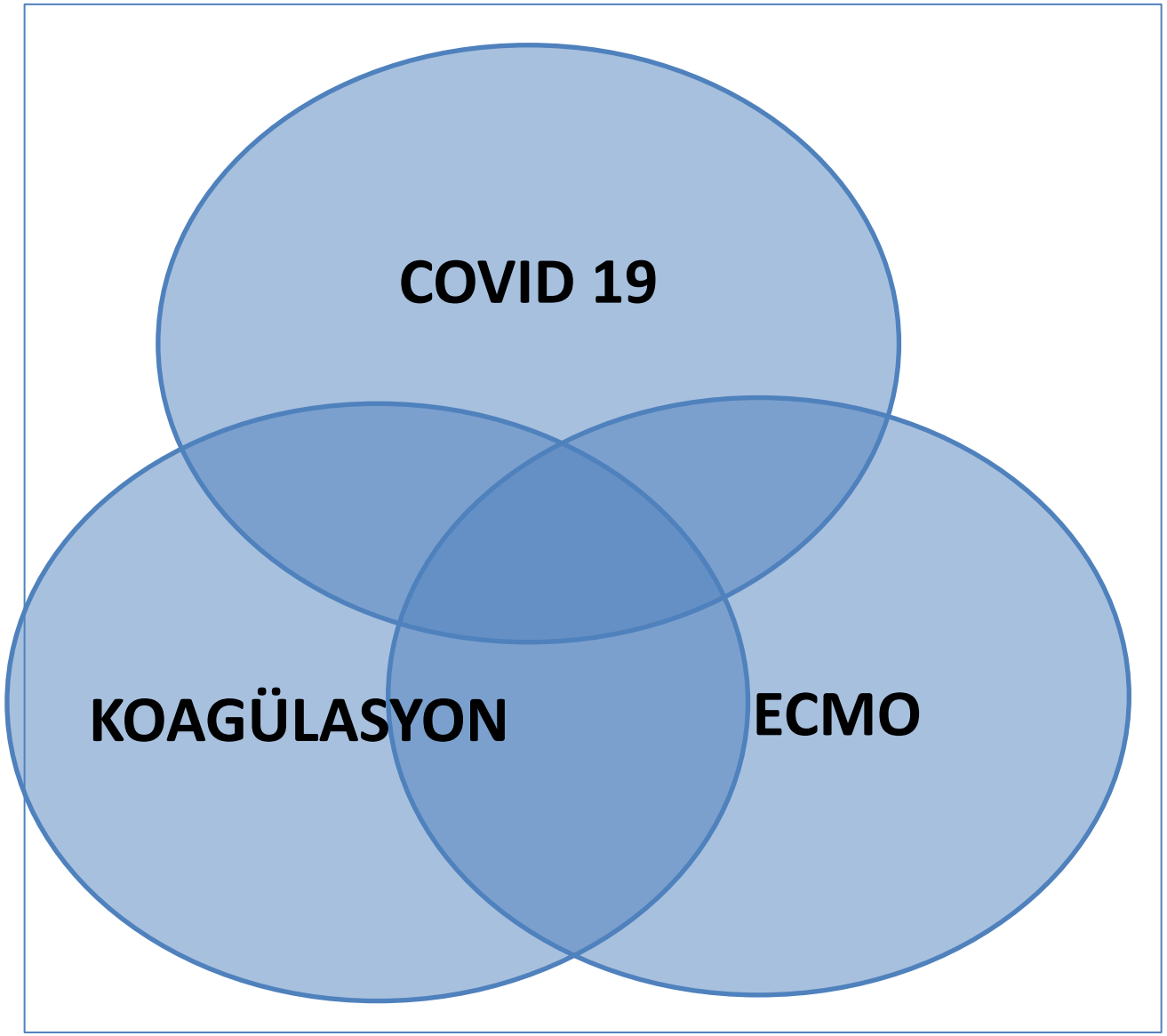
Study group	Data collection/ population	ECMO pts/total H1N1 pts.	Age of ECMO pts. (years)	PaO2/FIO2[a] (mmHg)	MV duration[a] (days)	ECMO duration (days)	Discharged alive[b], *n* (%)
ANZ ECMO Influenza Investigator [40]	Retrospective/15 ICUs	68/194	34.4 (26.6–43.1)	56 (48–63)	NA	10 (7–15)	32 (47.1%)
UK ERP with SwiFT study [41]	Prospective/4 centres	75[c]	36.5 ± 11.4	54.9 ± 14.3	4.4 ± 3.7	NA	57 (76%)
Italian ECMO network [42]	Prospective/14 ICUs	60/153	39 (32–46)	63.3 (56–79)	2 (1–5)	10 (7–17)	41 (68.3%)
Australian ERP [43]	Retrospective	38	NA	63	NA	NA	33 (86.8%)
Japanese Society [44]	Retrospective/12 ICUs	14	54	50 (40–55)	5 (0.8–8.5)	8.5 (4.0–10.8)	5 (35.73%)
REVA Research Network in France [45]	Prospective/114 ICUs	123	42 ± 13	63 ± 21	2 (1–5)	9.8	79 (64.2%)
Germany ARDS network [46]	Retrospective/40 centres	61/116	42 (39–45)[d]	87 (74–101)[d]	NA	NA	28 (45.9%)
Italian ECMO network [47]	Prospective/14 centres	60	39.7 ± 12	NA	NA	NA	41 (68.3%)

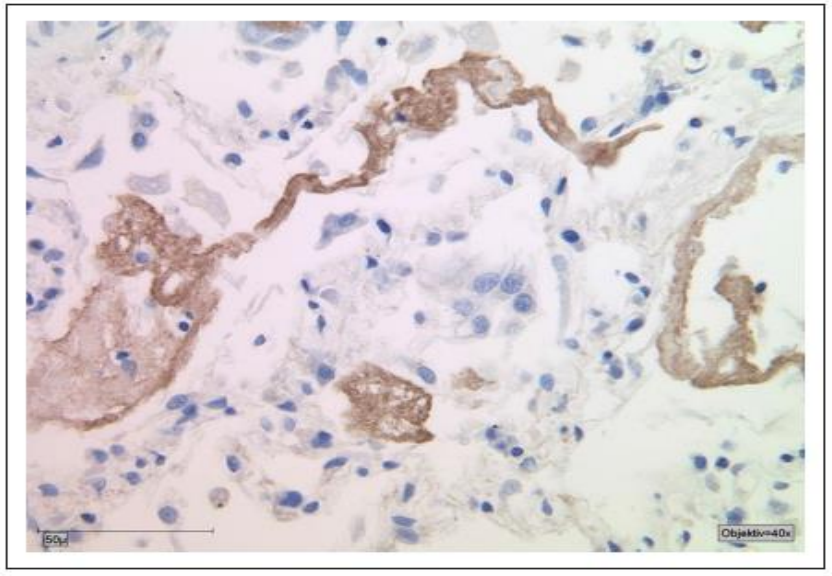
Table 3 Demographic data, the patient characteristics and ECMO data of 6 included studies with MERS outbreak (2012–2015)

First author	Country	Study design	Study population	ECMO pts./ total pts.	Age of ECMO pts. (years)	PaO2/FIO2[a] (mmHg)	MV duration[a] (days)	ECMO duration (days)	Discharged alive[b], *n* (%)
Choi WS [10]	South Korea	Retrospective/ multicentre	Ward and ICU	13/186	NA	NA	NA	NA	8 (61.5%)
Rhee JY [11]		Case review/ single centre	Ward and ICU	1/5	35	53	0 (4 h)	6	0
Al-Dorzi HM [12]	Saudi Arabia	Prospective/ single centre	HCW in ICU	1/8	NA	NA	NA	15	0
Arabi YM [13]		Retrospective/ multicentre	ICU	19/330	NA	NA	NA	NA	6 (31.6%)
Alshahrani MS [14]		Retrospective/ multicentre	ICU	17/35	45.5 (28.5–58.5)	NA	NA	NA	6 (35.3%)
Shalhoub S [15]		Retrospective/ multicentre	HCW in ward and ICU	9/32	NA	NA	NA	NA	4 (44.4%)

Geçmiş salgınlarda kullanılan ECMO'nun günümüz pandemisinde yararlı olup olamayacağı konusunda elimizde net bir veri yok. Ancak yarar/zarar oranı hasta özelinde değerlendirilmelidir.

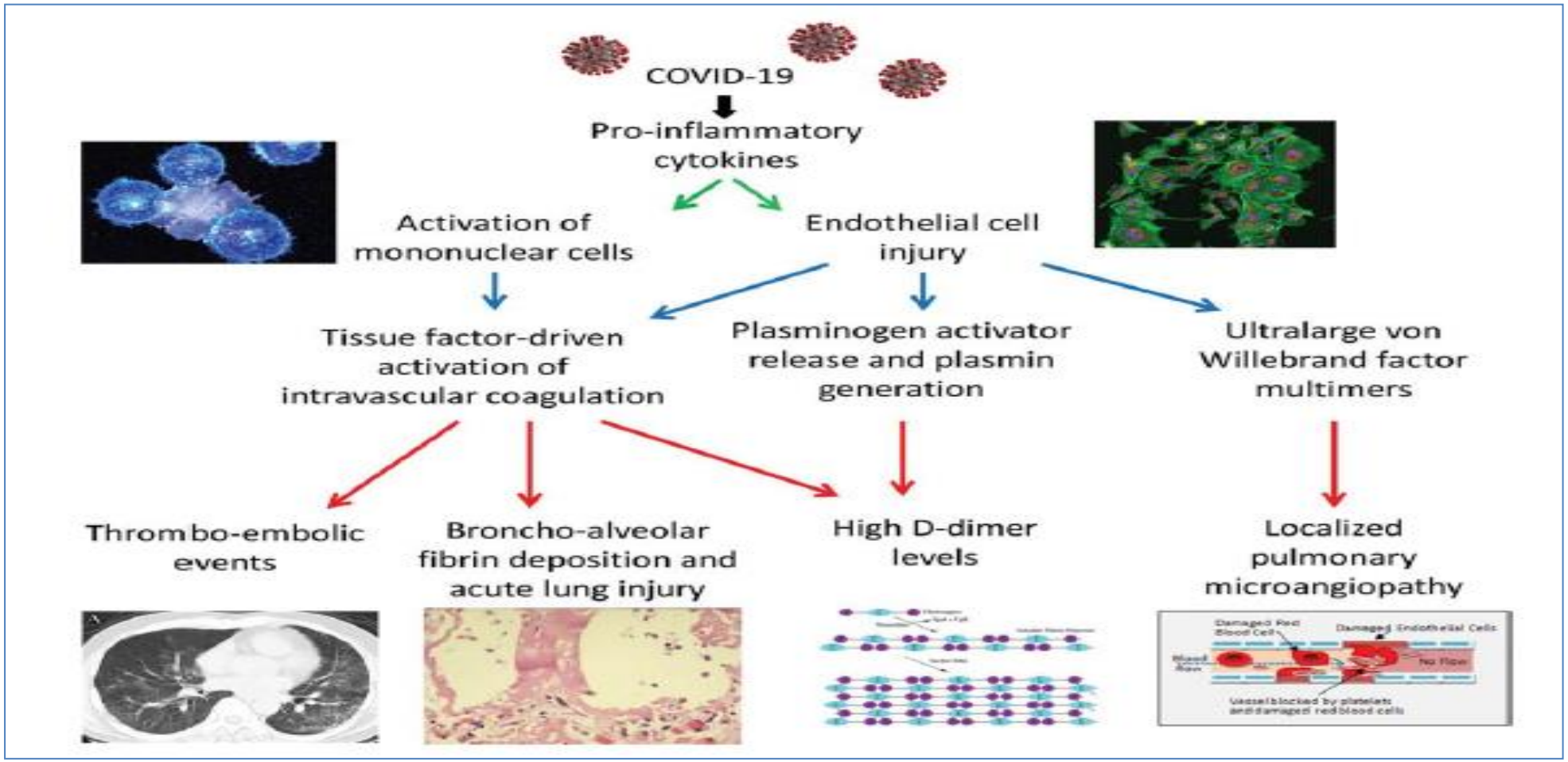
	EOLIA	LİFEGUARD	COVID 19 - ECMO
Day-60 Mortality	%35	%39	%31
Pre-ECMO P/F oranı	73	71	62
Complians	↓	↓	↓↓
Driving Pressure	↑	↑	↑↑
ECMO öncesi prone poziyondan yararlanma	%56	%26	%94
ECMO sırasında prone pozisyon kullanımı	%10	-	%81
Ventilatör ilişkili pnömoni oranı	%39	-	%87


COVID 19
KOAGÜLASYON
ECMO


50µ
Objektiv=40x

Coronavirus Disease 2019 Coagulopathy: Disseminated Intravascular Coagulation and Thrombotic Microangiopathy—Either, Neither, or Both

Marcel Levi, MD, PhD, FRCP[1,2] Jecko Thachil, MD, FRCP[3]



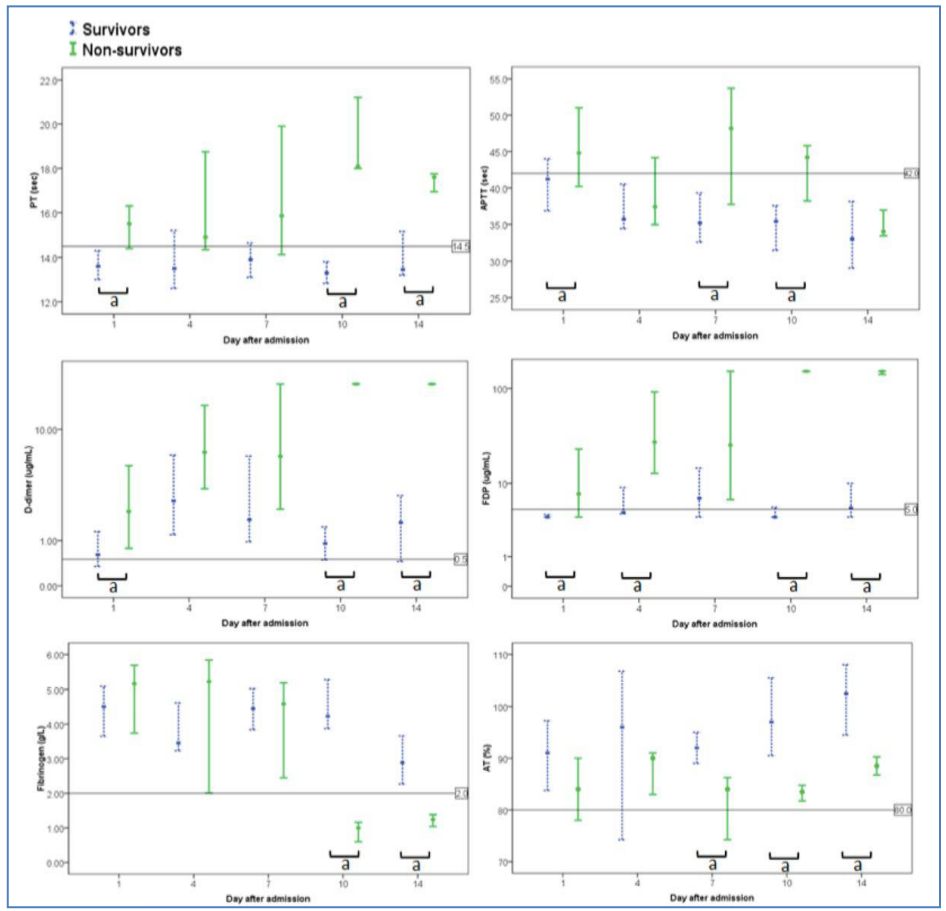
Received: 13 February 2020 | Accepted: 18 February 2020
DOI: 10.1111/jth.14768

BRIEF REPORT

jth

Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia

Ning Tang[1] | Dengju Li[2] | Xiong Wang[1] | Ziyong Sun[1]



SURVİVOR %0.6
NON SURVIVOR
%71.4

Protrombin zamanı (PT) ve aPTT normal veya hafifçe uzamış
Platelet sayıları normal / hafif trombositoz
Fibrinojen artmış
D-dimer artmış
Faktör VIII aktivitesi ve VWF antijen artmış

Review

Coagulation and anticoagulation in COVID-19

Tarik Hadid [a, b, *], Zyad Kafri [a, b], Ayad Al-Katib [a]

[a] Department of Internal Medicine, Wayne State University, School of Medicine, Detroit, MI, USA
[b] Ascension Michigan, Detroit, MI, USA

Table 1

Difference in coagulation parameters between COVID-19 and conventional sepsis.

Variable	COVID-19 sepsis	Conventional sepsis
aPTT	N/↑	↑↑/↑↑↑
PT	N/↑	↑↑/↑↑↑
Fibrinogen	↑↑↑/↑↑/↓	↑↑↑/↑↑/↓
Thrombocytopenia	N/↓	↓↓/↓↓↓
FSP	↑/↑↑	↑↑/↑↑↑
D-Dimer	↑↑/↑↑↑	↑/↑↑
Schistocytes on peripheral blood smear	Not present	Frequent

Hypercoagulability of COVID-19 patients in intensive care unit: A report of thromboelastography findings and other parameters of hemostasis

Mauro Panigada[1] | Nicola Bottino[1] | Paola Tagliabue[1] | Giacomo Grasselli[2] | Cristina Novembrino[3] | Veena Chantarangkul[3] | Antonio Pesenti[1,2] | Flora Peyvandi[2,3] | Armando Tripodi[3]

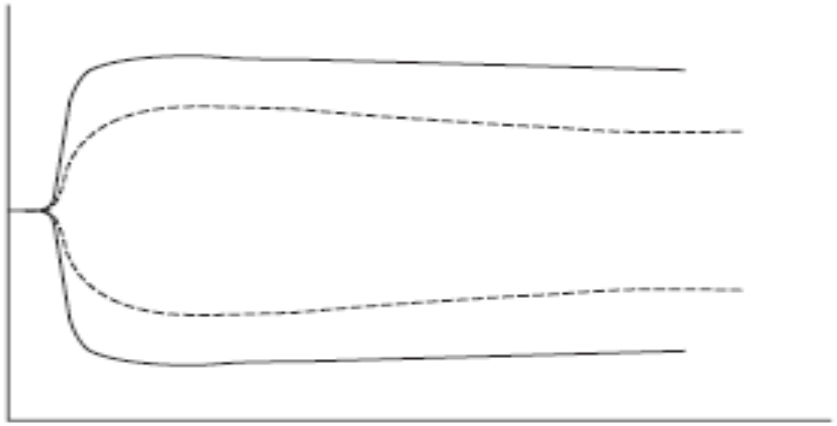
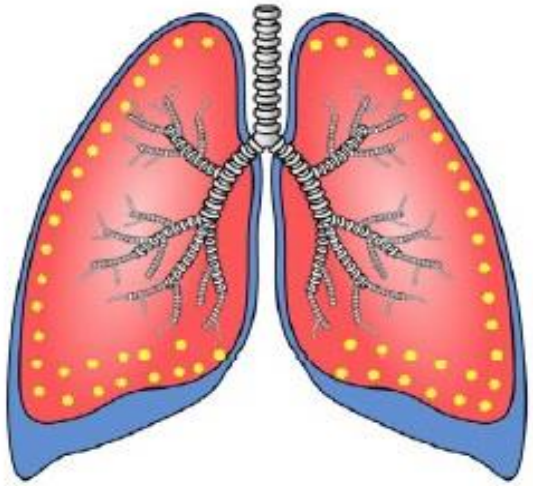
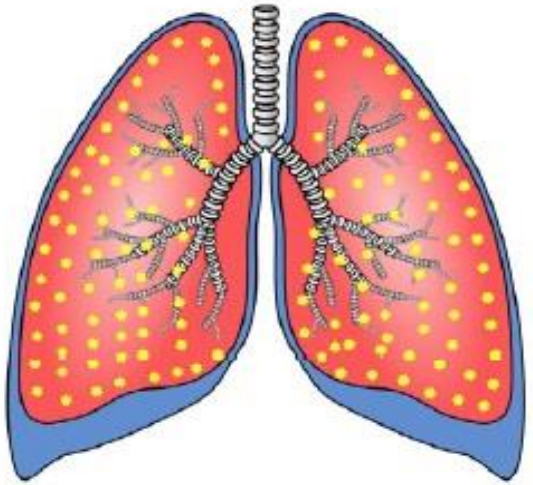
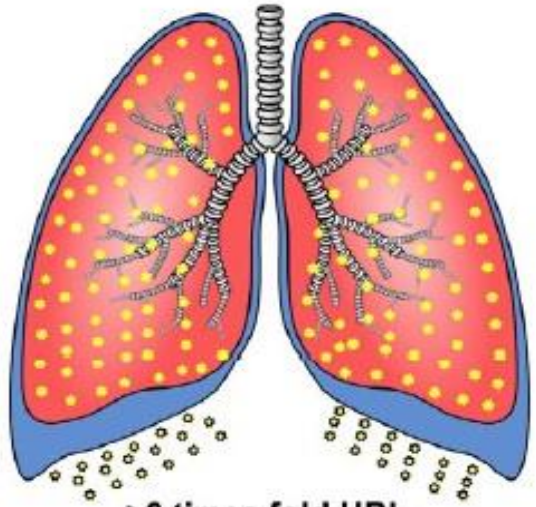


FIGURE 2 Typical TEG tracings. Upper and lower lines represent a healthy subject and a COVID-19 patient, respectively. The COVID-19 patient was characterized by the following TEG parameters: R = 5.5 minutes. K = 0.9 minutes. Angle K = 78.8°. MA = 88.8 mm and by the following hemostasis parameters: Prothrombin time ratio = 1.19. Activated partial thromboplastin time ratio = 1.21. D-dimer = 1829 ng/mL. Fibrinogen = 849 mg/dL. Antithrombin = 87 U/dL; Protein C = 116 U/dL. Protein S (free antigen) = 68 U/dL. Factor VIII = 269 U/dL. von Willebrand factor (antigen) = 476 U/dL. von Willebrand factor (ristocetin cofactor) = 347 U/dL. Platelet count = 546 × 10^9/L

Essentials

- COVID-19 is associated with a derangement of hemostasis, described as DIC.
- COVID-19 is associated with hypercoagulability as shown by thromboelastography.
- COVID-19 patients are candidate to antithrombotic prophylaxis/treatment.
- Clinical trials are urgently needed to establish appropriate antithrombotic regime.

	STAGE 1	STAGE 2	STAGE 3
			
D-dimer*	**2 to 3 times fold URL**	**3 to 6 times fold URL**	**>6 times fold URL**
Platelet count*	**Normal**	**100 to 150 x10^9/L**	**< 100 x10^9/L**
PT (aPTT)*	**Normal**	**Minimally prolonged**	**May be markedly prolonged**
Fibrinogen	Increased	Increased	Decreased
Inflammation	Local	Systemic	Hyperinflammation
DIC	Not present	Not present	May be present
Plasminogen activity	Increased	Moderately increased	Relative deficiency

Increase of bleeding and death risk

Time of evolution & place	Ward	Ward/HDU/ICU	IMV & ICU ± ECMO
Experimental therapy	Systematic LMWH prophylaxis vs. weight LMWH based vs. full dose LMWH	Systematic regular vs. double dose LMWH prophylaxis vs. full dose LMWH. Inhibition of contact system activation	Systematic double dose LMWH prophylaxis vs. full dose LMWH Thrombolysis

J Am Heart Assoc. 2021;10:e019650. DOI: 10.1161/JAHA.120.019650

Full Length Article

Venous thromboembolism in patients with COVID-19: Systematic review and meta-analysis

Angelo Porfidia[a,1], Emanuele Valeriani[b,c,1,*], Roberto Pola[a], Ettore Porreca[b], Anne W.S. Rutjes[d], Marcello Di Nisio[e]

30 çalışma, 3487 hasta
VTE insidansı %26
YBÜ hastalarının %24'ünde VTE gelişiyor (%19 PE)

VTE profilaksisi öneriliyor
Tedavi dozunda antikoagülasyon için yeterli kanıt yok/rutin kullanımı önerilmiyor

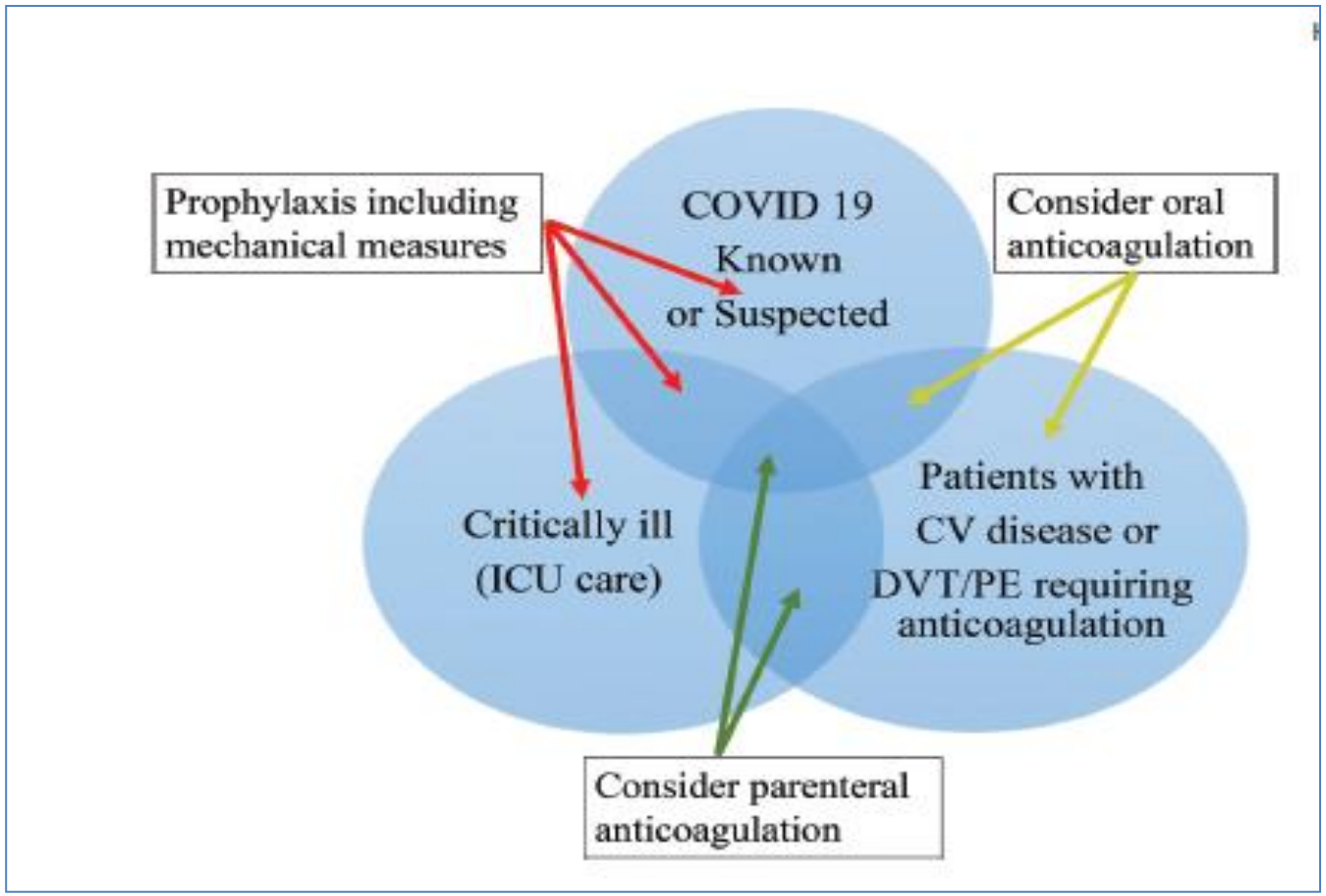
*Thrombosis Research 2020; 196:67-74.

CLINICAL FOCUS: INFECTIOUS DISEASES
REVIEW

Anti-coagulant and anti-platelet therapy in the COVID-19 patient: a best practices quality initiative across a large health system

Ryan A. Watson* [a], Drew M. Johnson* [a], Robin N. Dharia [b], Geno J. Merli [c] and John U. Doherty [a]

[a]Division of Cardiology, Department of Medicine, At Thomas Jefferson University Hospital, Sidney Kimmel Medical College, Philadelphia, PA, USA; [b]Division of Cerebrovascular Disease, Department of Neurology, Thomas Jefferson University Hospital, Sidney Kimmel Medical College, Philadelphia, PA, USA; [c]Division of Vascular Medicine, Department of Surgery and Medicine, Thomas Jefferson University Hospital, Sidney Kimmel Medical College, Philadelphia, PA, USA



COVID 19 VE ANTİKOAGÜLAN TEDAVİ

Uluslararası dernekler hastaneye yatan her hasta için kontrendikasyon yoksa antikoagülan tedavi (DMAH veya standart unfraksiyone heparin) ile tromboz proflaksisi öneriyor.

Ağır olmayan COVID-19

BMI <40kg/m2: Enoksaparin 40mg/gün sc

BMI > 40/kg/m2 Enoksaparin 40mg 2x1 sc

CrCl < 30ml/dak. : Enoksaparin kullanılması önerilmez. Standat heparin önerilir. 5000 U sc 2x1 veya 3 x1

Ağır COVID-19

CrCl> 30 ml/dak enoxaparin 40mg 2x1sc, veya standart heparin 7500 U/; 3x1

COVID 19 VE ANTİAGREGAN TEDAVİ

Şu anda COVID-19 hastalarında arteriyel tromboembolizm profilaksisi için aspirin kullanımını destekleyen herhangi bir kılavuz yok, ancak antitrombositlerle çalışmalar planlanmış veya devam etmekte

COVID 19 VE ANTİKOAGÜLAN TEDAVİ

Eculizumab-anti-C5 monoklonal antikor

Seksen kritik COVID-19 hastası ile yapılan bir çalışma (45'i eculizumab ve diğerleri standart tedavi) eculizumabın sağ kalımı iyileştirebileceğini ve hipoksiyi azaltabileceğini öne sürdü.

Bu ilacın kullanılabilmesi için etkililiğini ve güvenliğini değerlendiren randomize kontrollü çalışmalara ihtiyaç var (SOLID-C19 çalışma sonuçları bekleniyor)***

Anticoagulation in COVID-19: Effect of Enoxaparin, Heparin, and Apixaban on Mortality

Henny H. Billett[1,*] Morayma Reyes-Gil[2,*] James Szymanski[2] Kenji Ikemura[2] Lindsay R. Stahl[3] Yungtai Lo[4] Shafia Rahman[1] Jesus D. Gonzalez-Lugo[1] Margarita Kushnir[1] Mohammad Barouqa[2] Ladan Golestaneh[5] Eran Bellin[4,*]

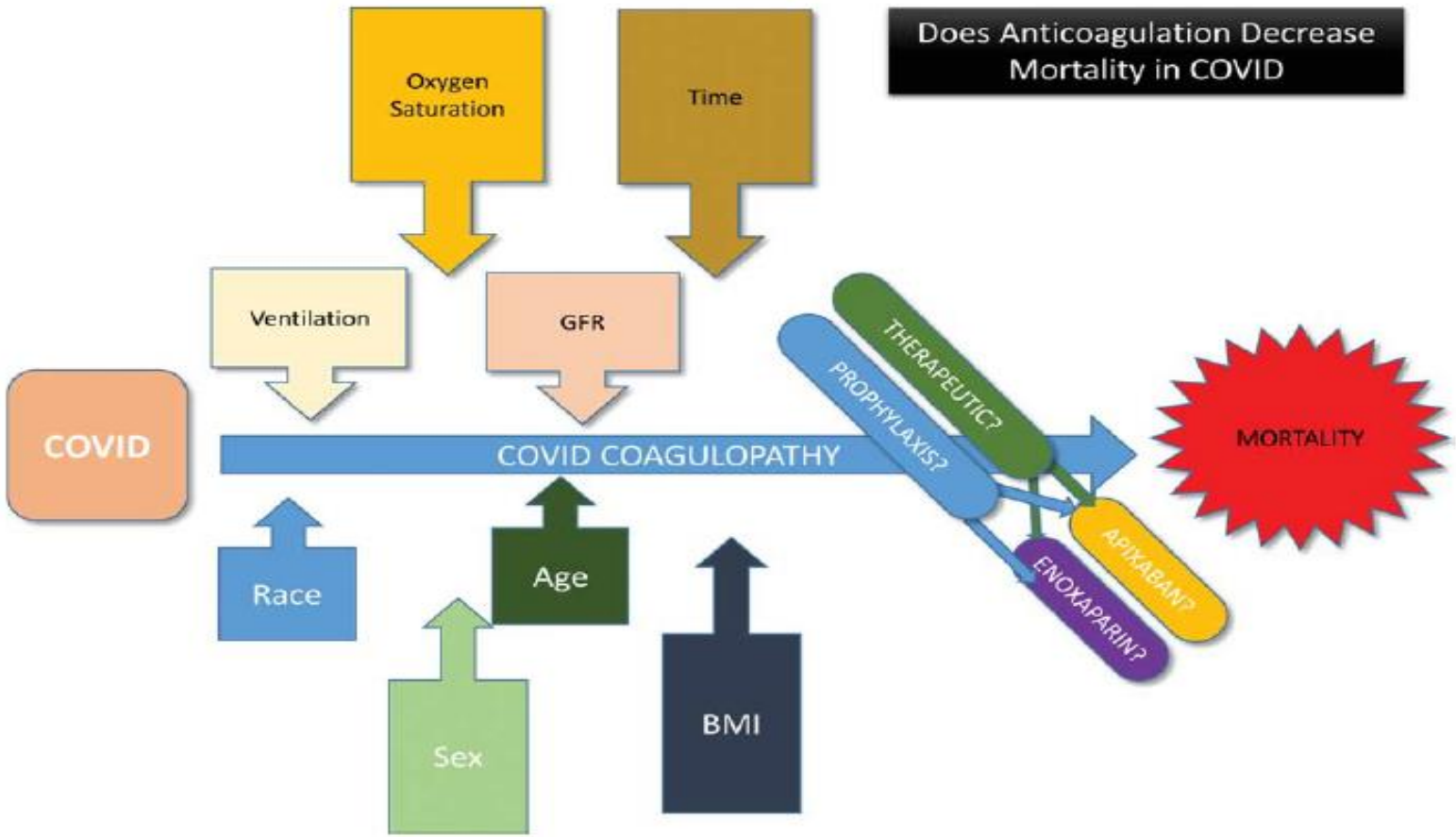
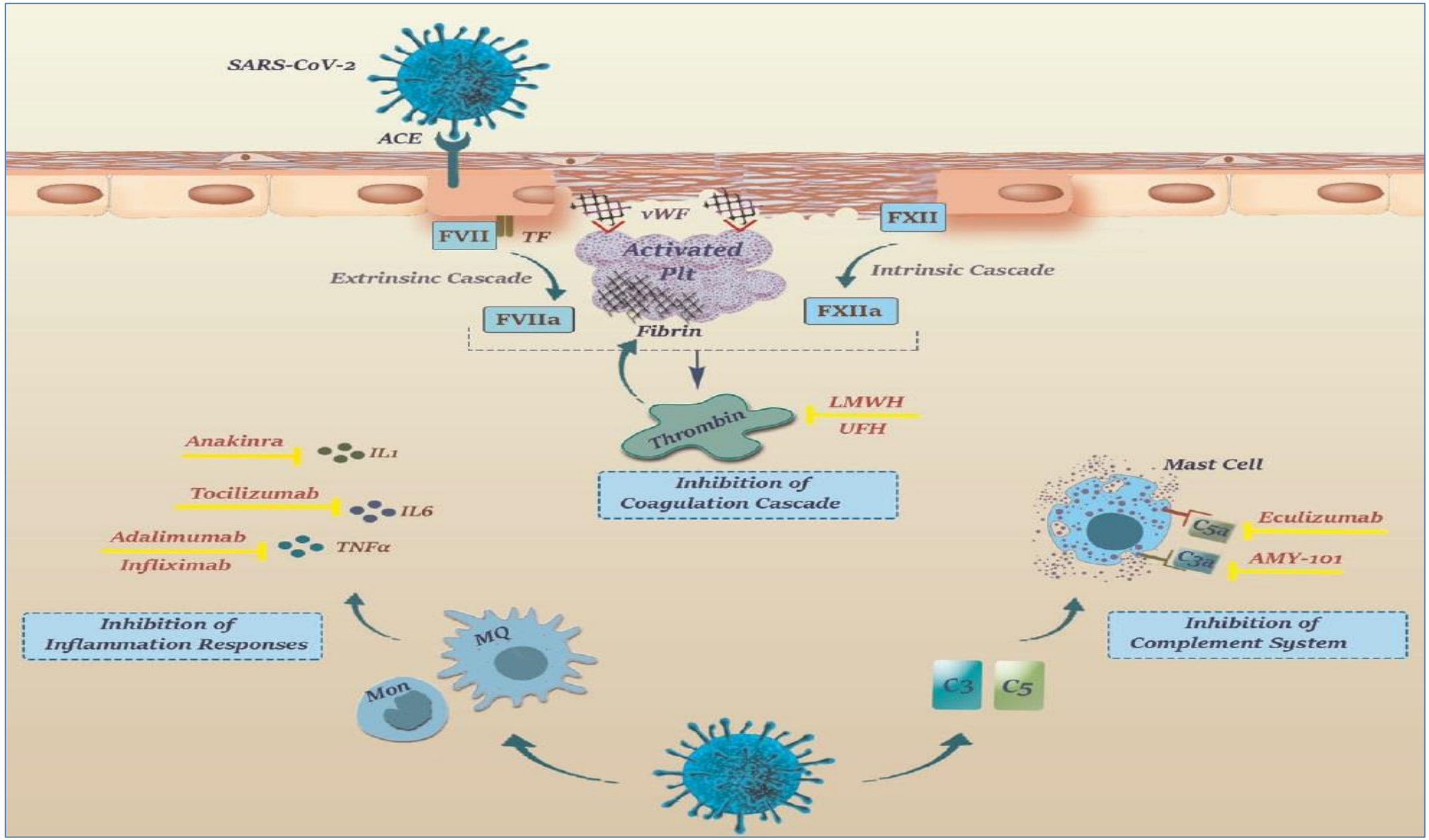


Fig. 2 Visual Summary: Does anticoagulation decrease mortality in coronavirus disease.


SARS-CoV-2
ACE
vWF
FVII
TF
FXII
Activated Plt
Extrinsinc Cascade
Intrinsic Cascade
FVIIa
FXIIa
Fibrin
Thrombin
LMWH
UFH
Inhibition of Coagulation Cascade
Anakinra
IL1
Tocilizumab
IL6
Adalimumab
Infliximab
TNFα
Inhibition of Inflammation Responses
MQ
Mon
C3
C5
Mast Cell
C5a
C3a
Eculizumab
AMY-101
Inhibition of Complement System

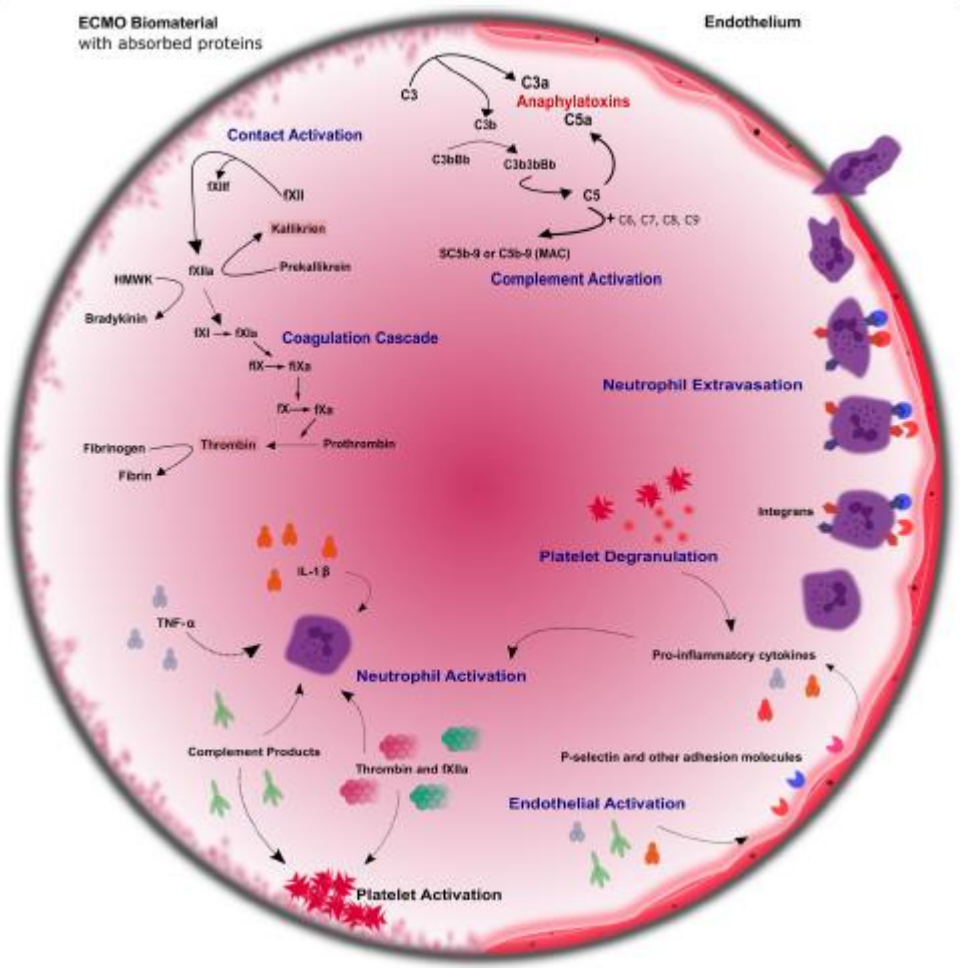
Millar et al. Critical Care (2016) 20:387
DOI 10.1186/s13054-016-1570-4

Critical Care

REVIEW Open Access

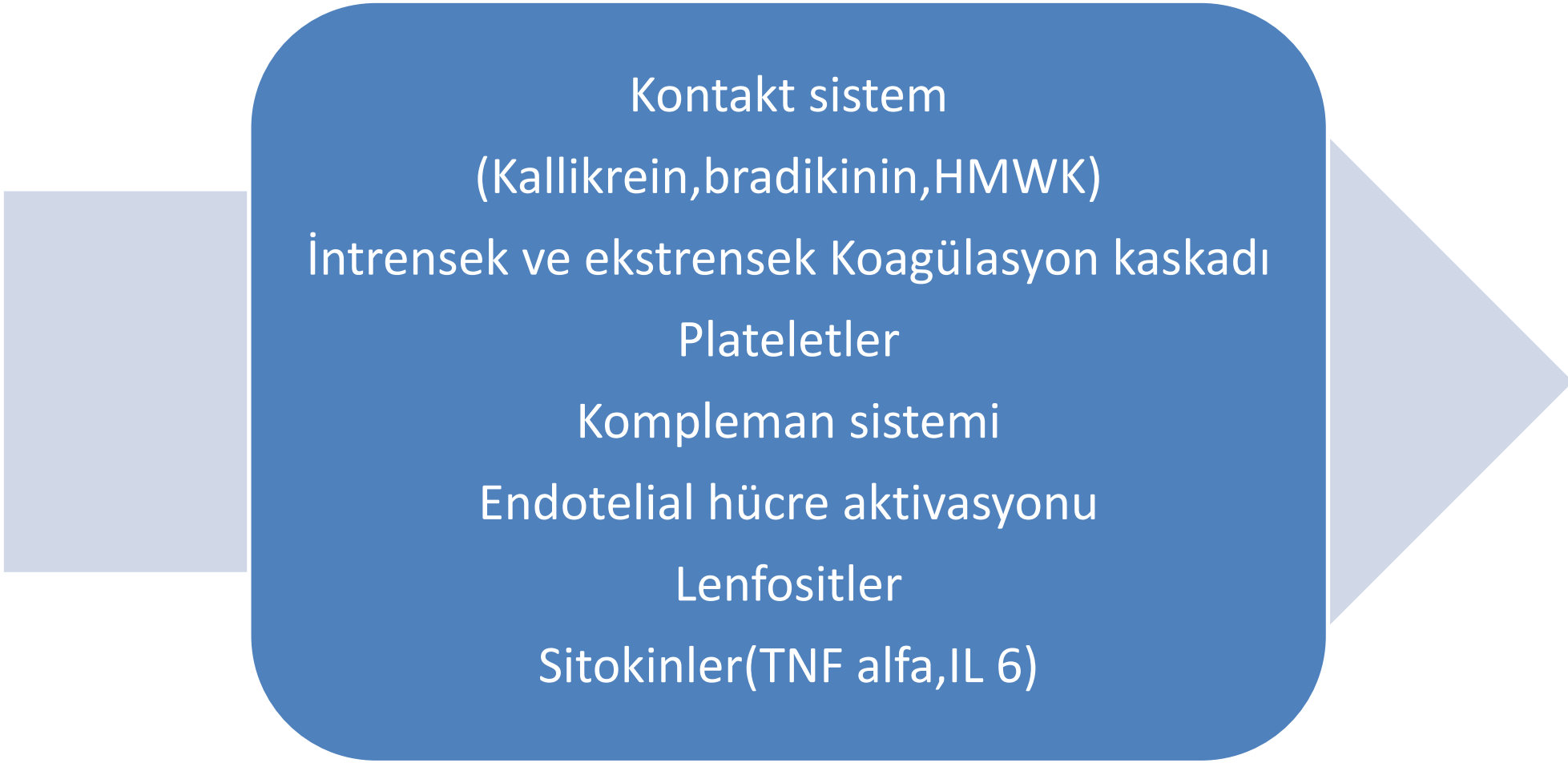
The inflammatory response to extracorporeal membrane oxygenation (ECMO): a review of the pathophysiology

Jonathan E. Millar[1,3*], Jonathon P. Fanning[1], Charles I. McDonald[1], Daniel F. McAuley[2] and John F. Fraser[1]



The inflammatory response to ECMO is complex and multi-faceted. It remains unclear whether this excess inflammation is all deleterious, or if it has potential benefits to the host. In summary, it arises principally due to the contact and complement systems becoming activated as a result of blood exposure to the extracorporeal circuit. The combination of a sustained innate immune response and the pro-inflammatory aspects of coagulation result in "pan-endothelial" injury, with leukocyte activation and the production of pro-inflammatory mediators. This ultimately ends in a systemic inflammatory response and end-organ damage.

ECMO ; Koagülasyon ve İnflamasyon Arasındaki İlişki



Bleeding and Thrombotic Complications in the Use of Extracorporeal Membrane Oxygenation

James Thomas, MD[1] Vadim Kostousov, MD[2] Jun Teruya, MD, DSc, FCAP[2,3]

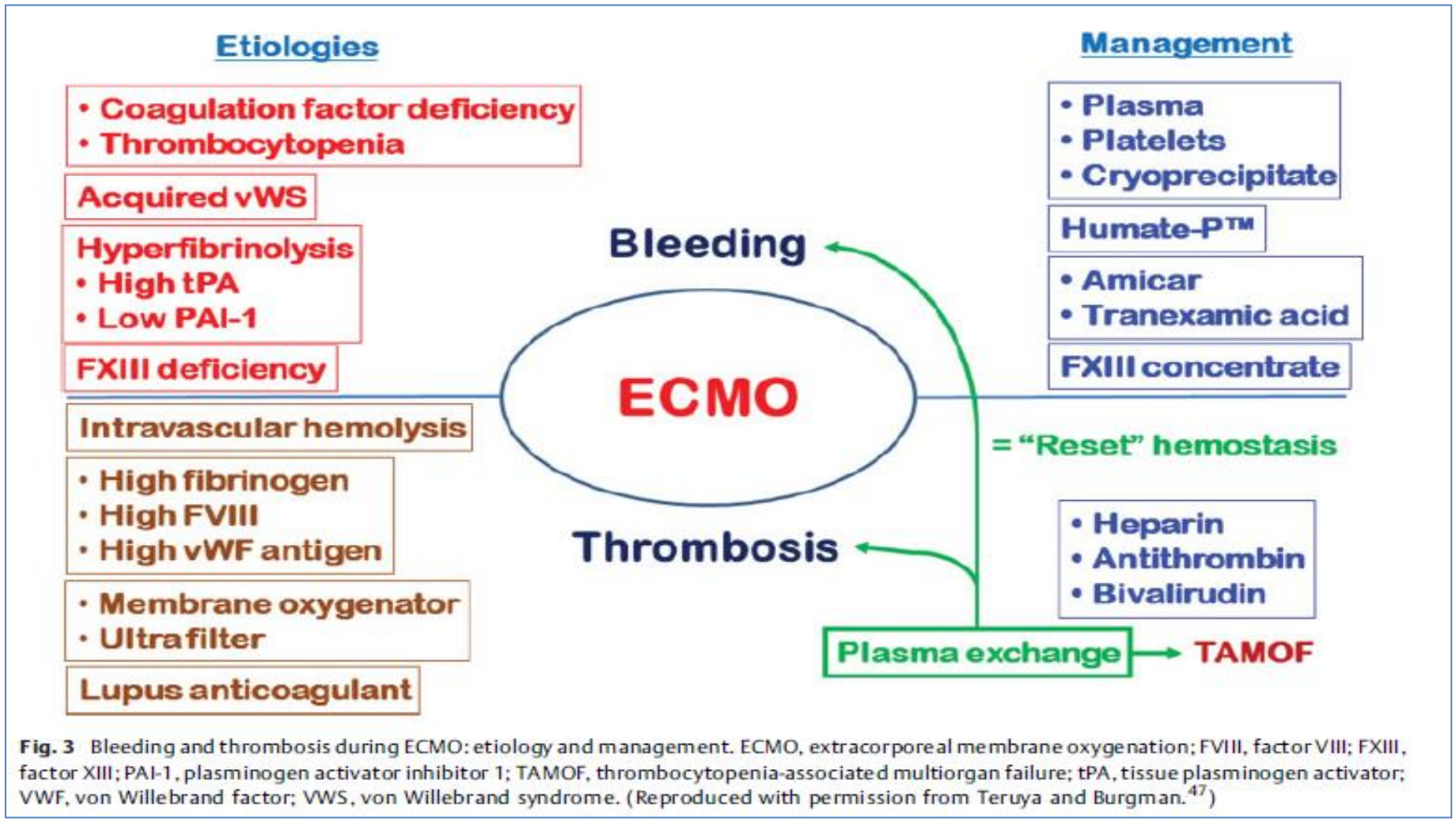


Fig. 3 Bleeding and thrombosis during ECMO: etiology and management. ECMO, extracorporeal membrane oxygenation; FVIII, factor VIII; FXIII, factor XIII; PAI-1, plasminogen activator inhibitor 1; TAMOF, thrombocytopenia-associated multiorgan failure; tPA, tissue plasminogen activator; VWF, von Willebrand factor; VWS, von Willebrand syndrome. (Reproduced with permission from Teruya and Burgman.[47])

Bleeding and Thrombotic Complications in the Use of Extracorporeal Membrane Oxygenation

James Thomas, MD[1] Vadim Kostousov, MD[2] Jun Teruya, MD, DSc, FCAP[2,3]

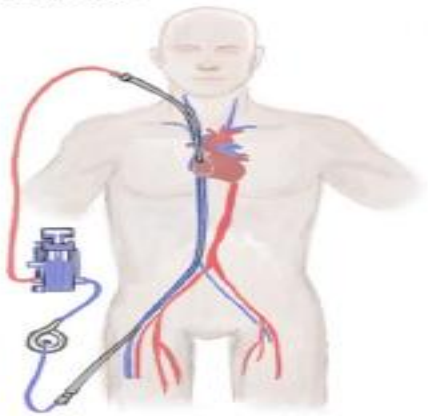
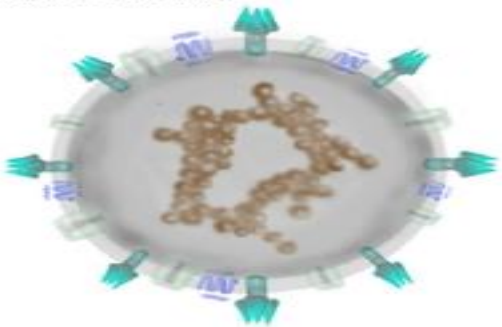
Test	Desired target/range	Purpose
PT	<16.0–17.0 s	To assess underlying coagulable state
aPTT with Dade Hepzyme	<38.0 s	
Fibrinogen	>200 mg/dL	
aPTT	70–90 s	To monitor heparin effect
D-dimer	Not established	To monitor fibrin formation and fibrinolysis in the circuit and patient's circulation
Platelet count	>100,000/mm^{355}	To monitor clot firmness
Anti-FXa	0.2–0.5 units/mL	To monitor heparin activity
Antithrombin	>80–100%	To maximize heparin therapy

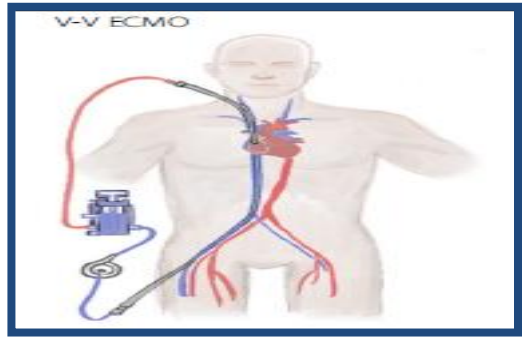
REVIEW Open Access

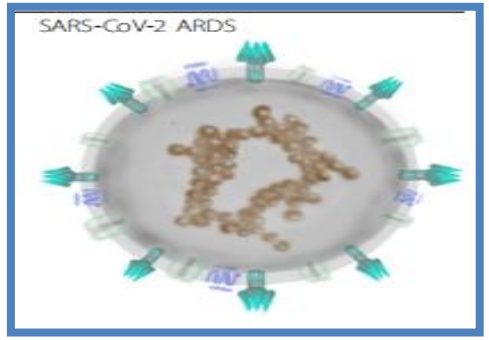
COVID-19 and ECMO: the interplay between coagulation and inflammation—a narrative review

Mariusz Kowalewski[1,2,3*†], Dario Fina[2,4†], Artur Słomka[5], Giuseppe Maria Raffa[6], Gennaro Martucci[7], Valeria Lo Coco[2,6], Maria Elena De Piero[2,8], Marco Ranucci[4], Piotr Suwalski[1] and Roberto Lorusso[2,9]

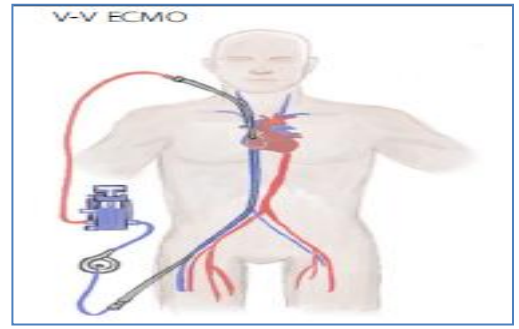
Table 1 Comparison of hematological and biochemical parameters in V-V ECMO and SARS-CoV-2 induced ARDS

	V-V ECMO	SARS-CoV-2 ARDS
		
Hematological findings		
White blood cell count	Initial ↑	↑
Lymphocyte	↓	↓↓
Neutrophil	Initial ↑	↑
Neutrophil activation	Initial ↑	?
Monocyte	Initial ↑	–
$CD3^+$, $CD4^+$, $CD8^+$, T cells	↓	↓↓
Natural killer cells	↓	– ↓
Neutrophil to lymphocyte ratio	↑	↑
Hemoglobin and red blood cell count	↓	–
Platelet count	↓	↓–





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	↑	?
FVIII	↓	?
FX	↑	?
FXI	↓	?
FXIa	↑	?
FXII	↓	?



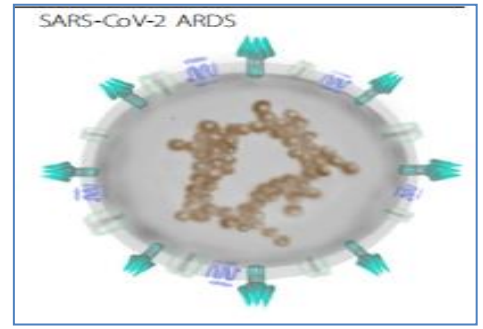


Table 1 Comparison of hematological and biochemical parameters in V-V ECMO and SARS-CoV-2 induced ARDS *(Continued)*

FXIIa	Rapid ↑	?
FXIII	↓	?
Antithrombin	Initially ↓ (UFH)	↓
C-protein	↑↓	?
Activated clotting time	↑	?
R-time thromboelastography	↑	?
Inflammatory response		
Tissue factor	↑–	?
Bradykinin	↑	?
TNF-alpha	↑	–↑
IFN-gamma	?	↑ (4–6 days after presentation)
IL-1-beta	↑	↓↓
IL-2	?	↑ 4–6 days after presentation
IL-2R	?	↑
IL-4	?	–
IL-6	↑	↑↑
IL-8	↑	?
IL-10	↑	↑
IgE	↓	?
IgA	?	–
IgG	?	–↑
IgM	?	–
Complement	–↑	–

Extracorporeal Membrane Oxygenation (ECMO) in Critically Ill Patients with Coronavirus Disease 2019 (COVID-19) Pneumonia and Acute Respiratory Distress Syndrome (ARDS)

Vital Questions of ECMO in COVID-19

1. Yeterli kanıt var mı?
2. Mortalite oranları hala çok yüksek
3. ECMO ne zaman uygulanmalı ?
4. Hangi ECMO modalitesi (VV,VAV,VA)
5. İmmonulojik faktörler(lenfosit sayısı ve IL 6) ECMO kullanımından olumsuz etkilenmekte

Conclusions

The highly contagious 2019-ConV has now infected tens of thousands of Chinese and has rapidly become a global pandemic, with health care systems overwhelmed with severe and critically ill patients in less well-resourced countries. ECMO is a sophisticated life support system supporting respiratory and circulatory failure and has been utilized in the management of severe infection with MERS and H1N1 influenza, with some evidence showing an additional survival benefit with use of ECMO. Much remains mysterious about the virus 2019-ConV, and solid clinical evidence is lacking on the role of ECMO in rescuing critical illness. Despite the application of ECMO in China and recommendations on ECMO by WHO and Chinese experts in COVID-19, several fundamental questions remain unanswered, including benefit, timing, indications, management, and risks of ECMO, as well as global sharing of evidence from trials.

Extracorporeal membrane oxygenation and COVID-19: The causes of failure

Abstract

Introduction: Venovenous extracorporeal membrane oxygenation (VV-ECMO) is a therapeutic strategy for the coronavirus disease 2019 (COVID-19) induced acute respiratory distress syndrome (ARDS). There are inconclusive data in this regard and causes of VV-ECMO failure are not yet understood well.

Case Series: Here, seven patients with COVID-19-induced ARDS who underwent VV-ECMO introduced and causes of VV-ECMO failure discussed. Medical records of seven COVID-19 patients treated with VV-ECMO were retrospectively evaluated to determine the clinical outcomes of VV-ECMO. Oxygenator failure occurred in four patients whom needed to oxygenator replacement. Successful VV-ECMO decannulation was done in three patients, however finally one patient survived.

Conclusions: Hypercoagulability state and oxygenator failure were the most main etiologies for VV-ECMO failure in our study. All patients with COVID-19 undergoing VV-ECMO should be monitored for such problems and highly specialized healthcare team should monitor the patients during VV-ECMO.

J Card Surg. 2020;1-6.

SONUÇ OLARAK

- Şiddetli COVID-19 hastalığıyla tromboembolizm arasında güçlü bir ilişki vardır.
- Trombotik komplikasyonlar morbidite ve mortalitenin başlıca nedenidir.
- ECMO uygulamalarının koagülasyon ve inflamasyon kaskadını olumsuz etkilediği unutulmamalıdır.
- COVID-19 ilişkili Ağır ARDS olgularında ECMO uygulaması koagülapati üzerine benzer olumsuz etkilere sahiptir.
- Heparin, bivaluridin antikoagülasyon için kullanılması daha önceki ECMO uygulamalarına benzer şekilde önerilmektedir.