ĐIỀU TRỊ CHỐNG HUYẾT KHỐI Ở BỆNH NHÂN COVID-19

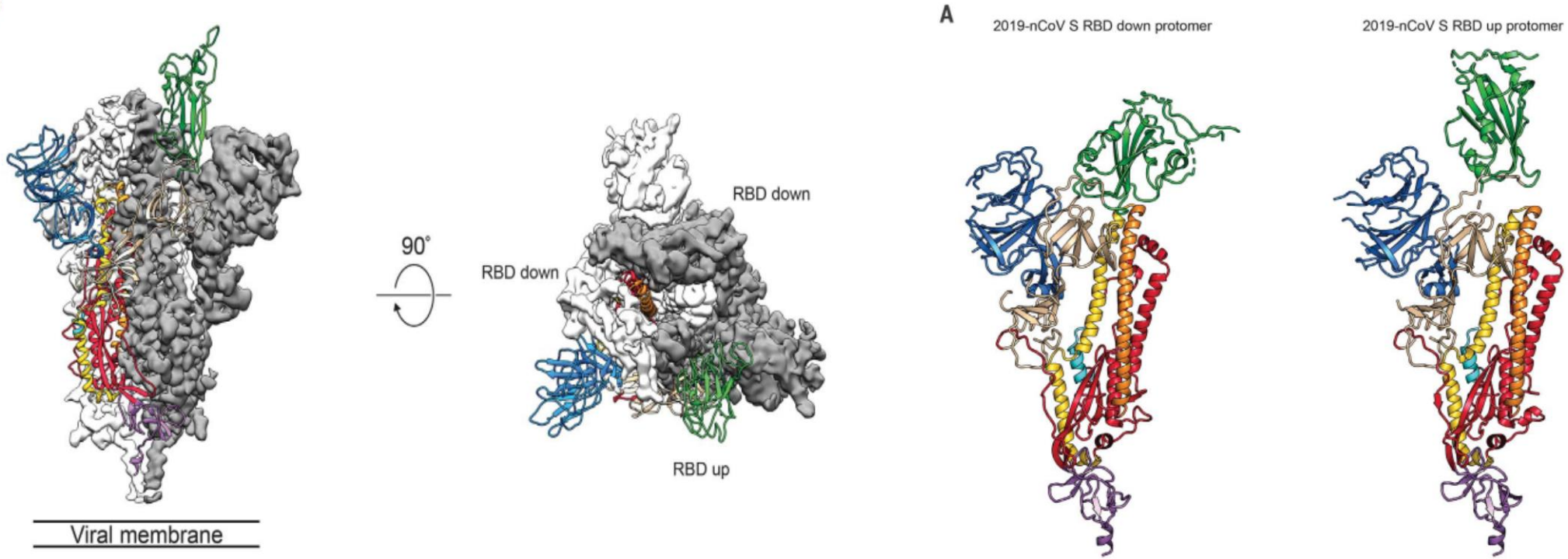
BS CKI. CAO THÀNH CHƯƠNG

BM HSCCCĐ– ĐHYD TP.HCM

NỘI DUNG CHÍNH

- CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19
- BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG CỦA HUYẾT KHỐI
- CÁC KHUYẾN CÁO VỀ ĐIỀU TRỊ CHỐNG HUYẾT KHỐI

CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19

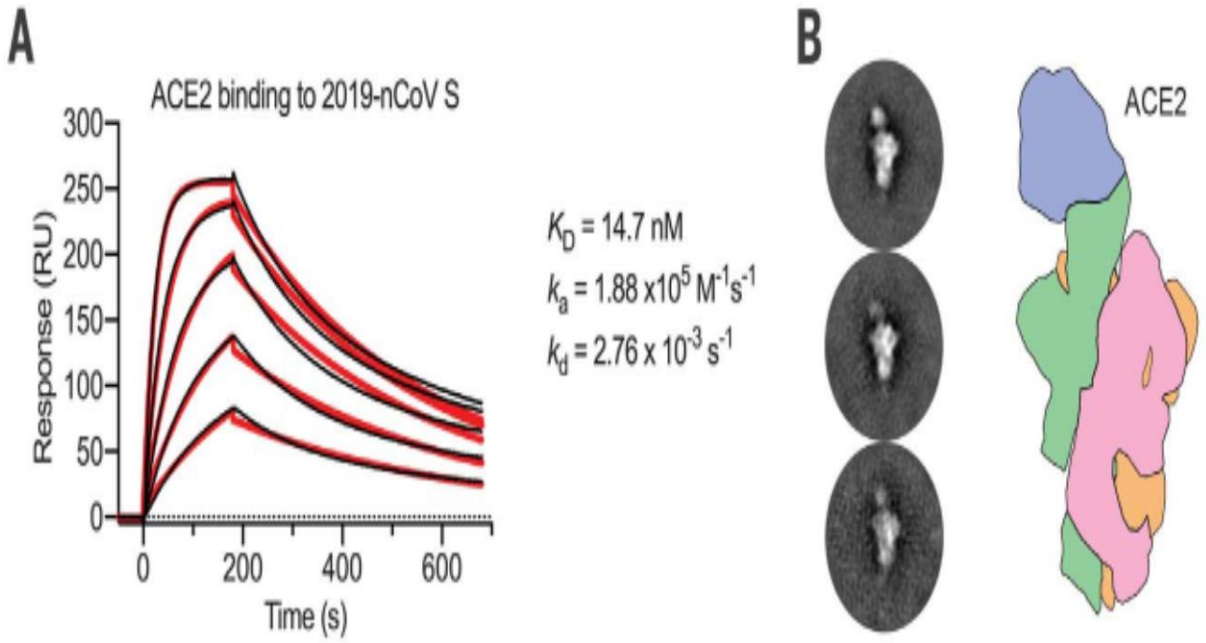


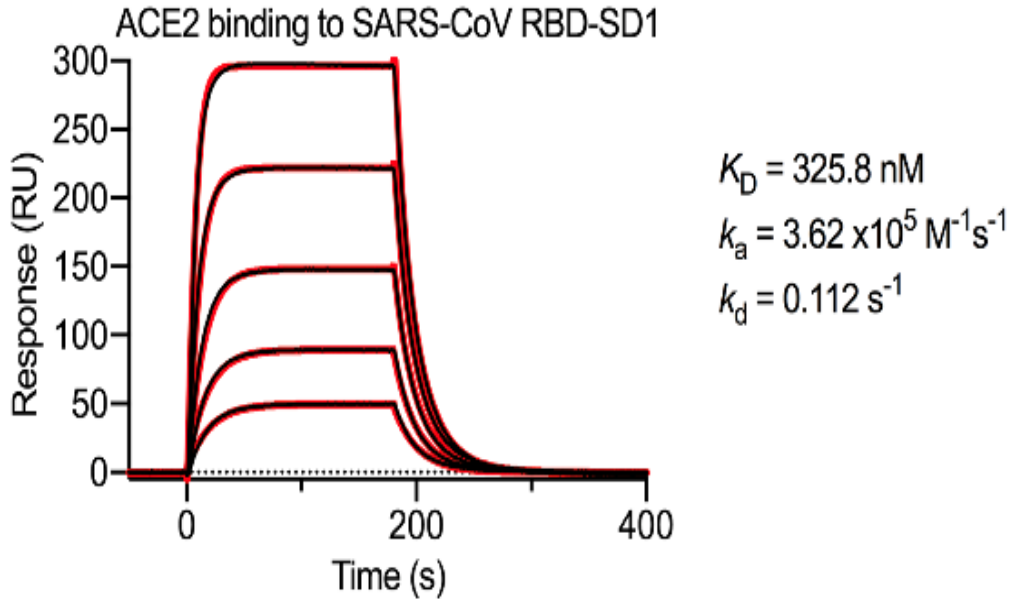
Cấu trúc của SARS-CoV 2 với bán đơn vị S1 chứa Receptor Binding Domain (RDB) có khả năng chuyển đổi 2 trạng thái "up" và "down"

Wrapp et al., Science 367, 1260–1263 (2020) 13 March 2020

CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19

VAI TRÒ GLYCOPROTEIN SPIKE (S) BỀ MẶT VÀ THỤ THỂ ACE2



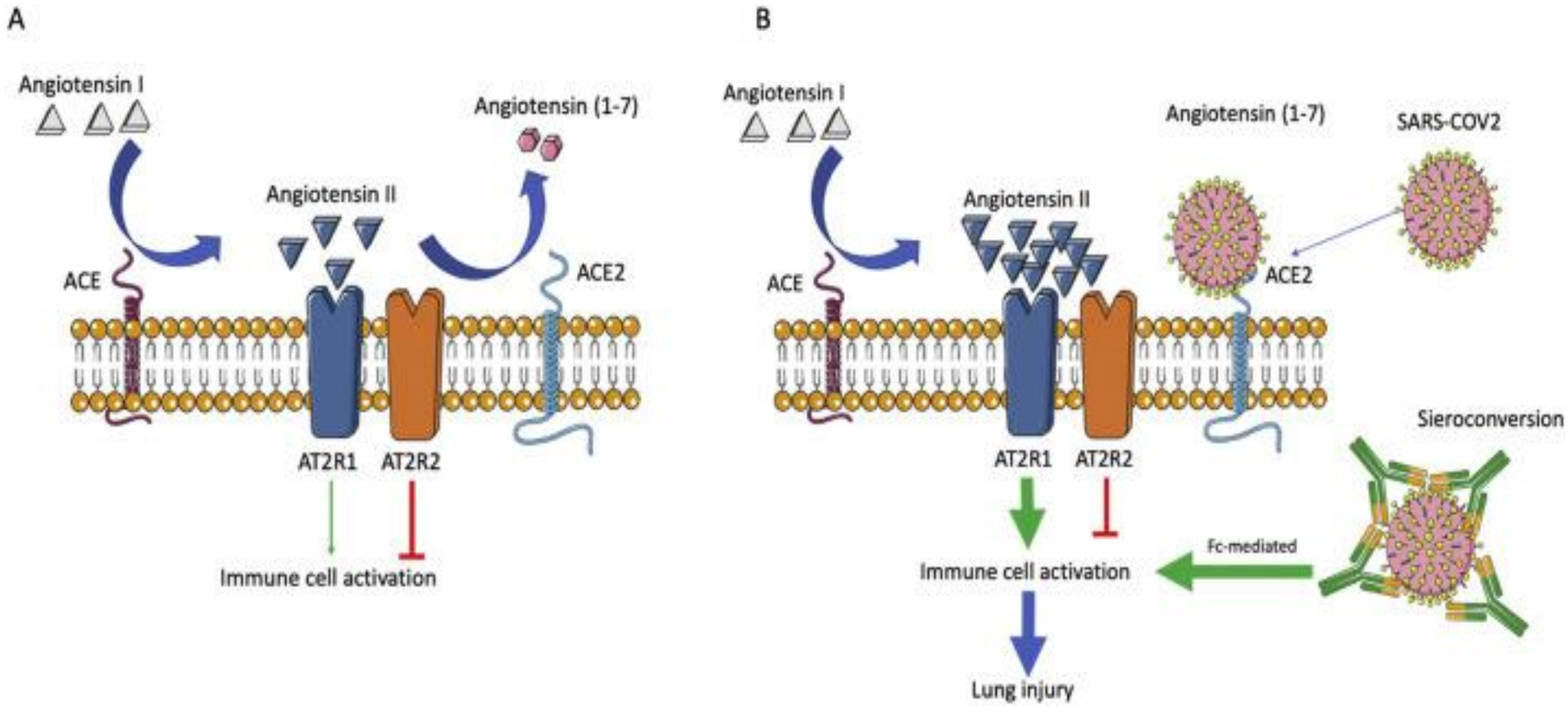


Ái lực của SARS-CoV 2 với thụ thể ACE2

Ái lực của SARS-CoV đối với thụ thể ACE2

Wrapp et al., Science 367, 1260–1263 (2020) 13 March 2020

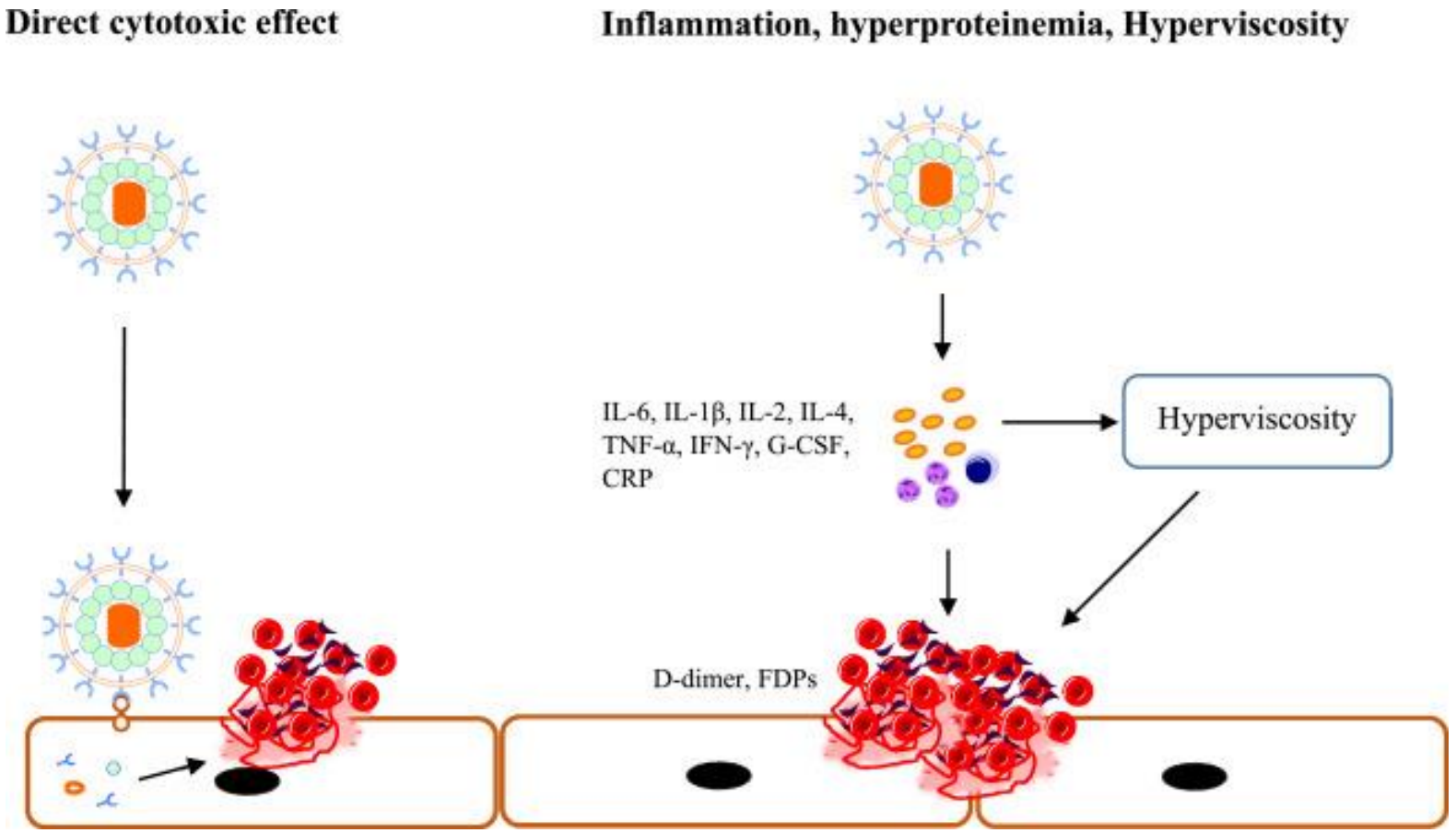
CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Vai trò của hệ RAA trong cơ chế bệnh sinh của SARS-CoV2

Felice R., 2020, Autoimmun Rev.

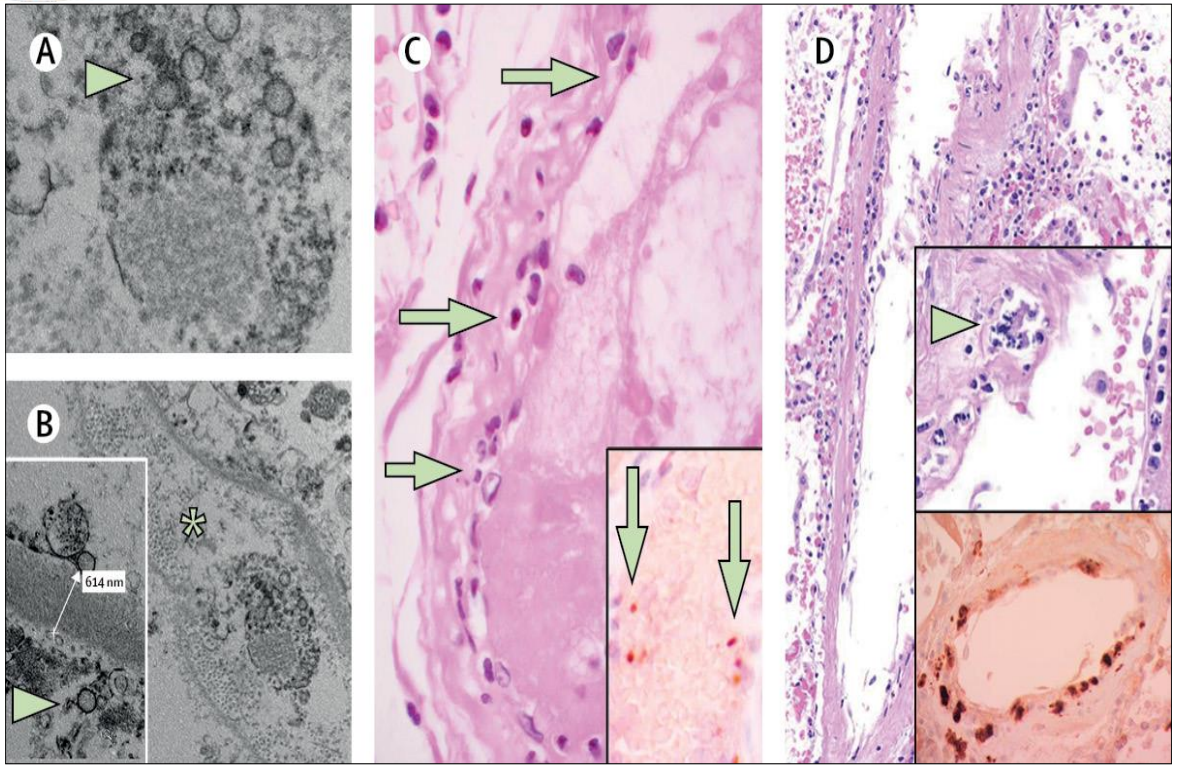
CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Cơ chế chính gây đông máu nội mạch do SARS-CoV2: tổn thương tế bào nội mô

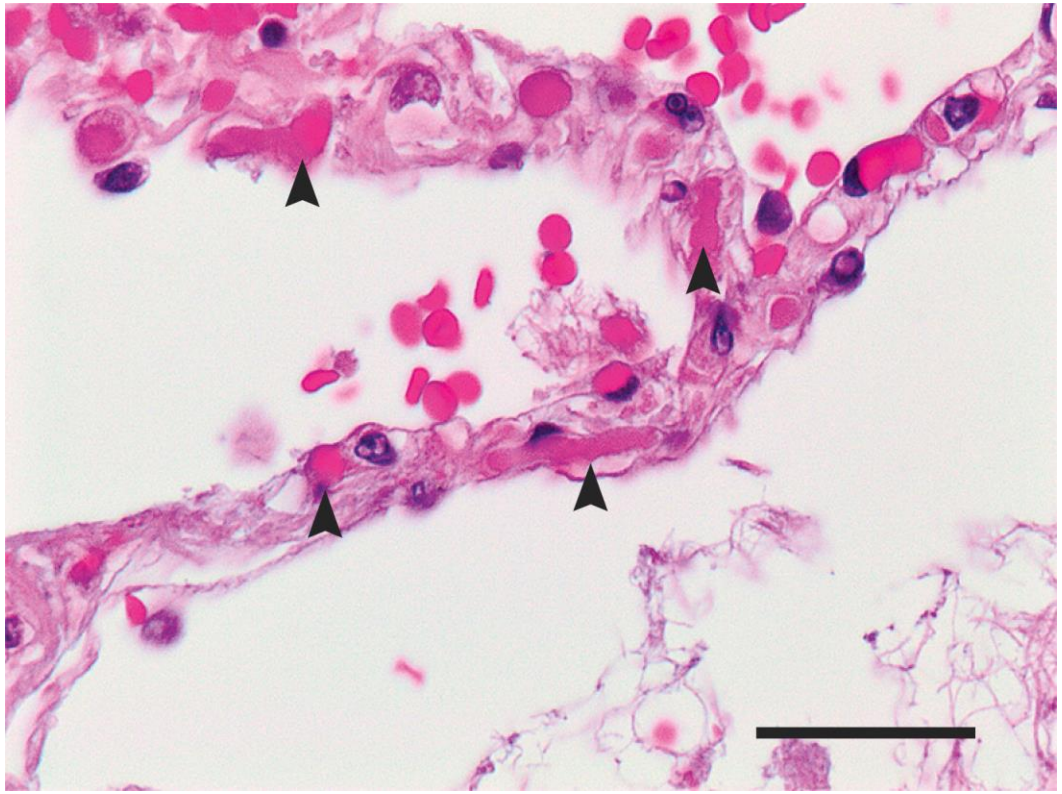
Joshua K. S. at al, 2021, Heart & Lung

CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Tổn thương tế bào nội mô do SARS-CoV2

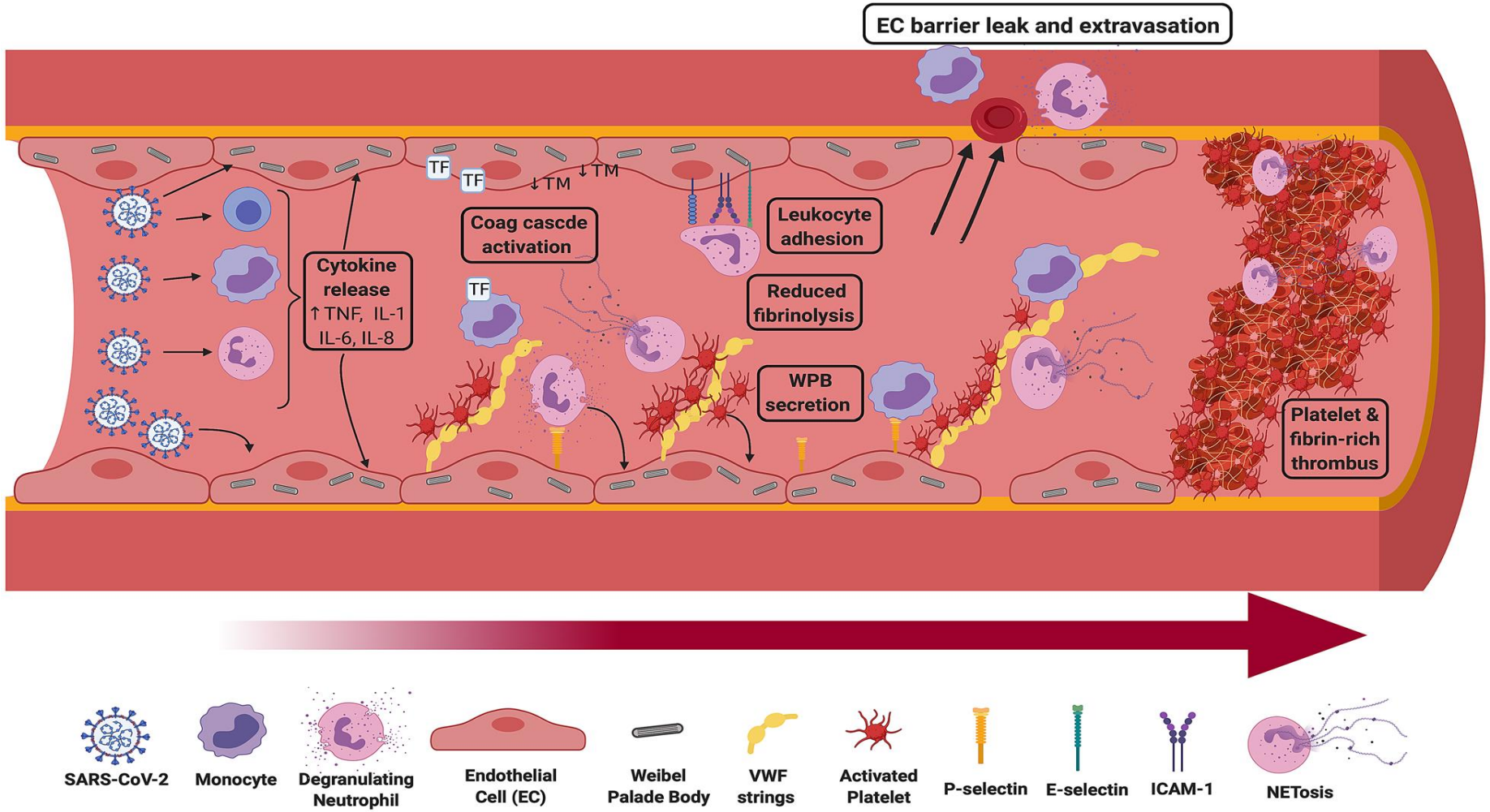
Zsuzsanna V., 2020, The Lancet



Vi huyết khối ở các vách gian phế nang phổi

Maximilian A., 2020, NEJM

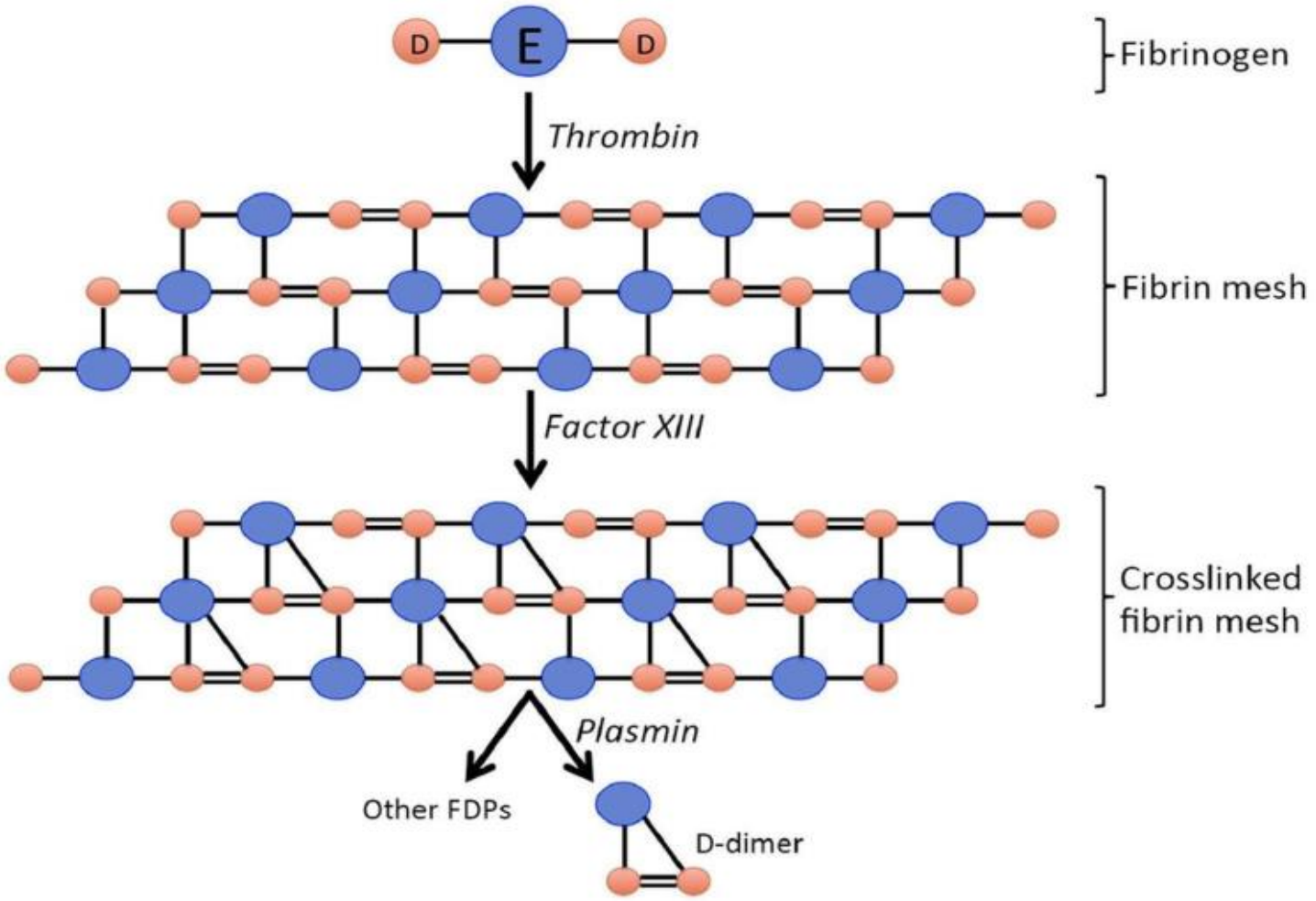
CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Cơ chế gây huyết khối miễn dịch ở phổi trên bệnh nhân ARDS do SARS-CoV2

James S. O., 2021, Intensive care med

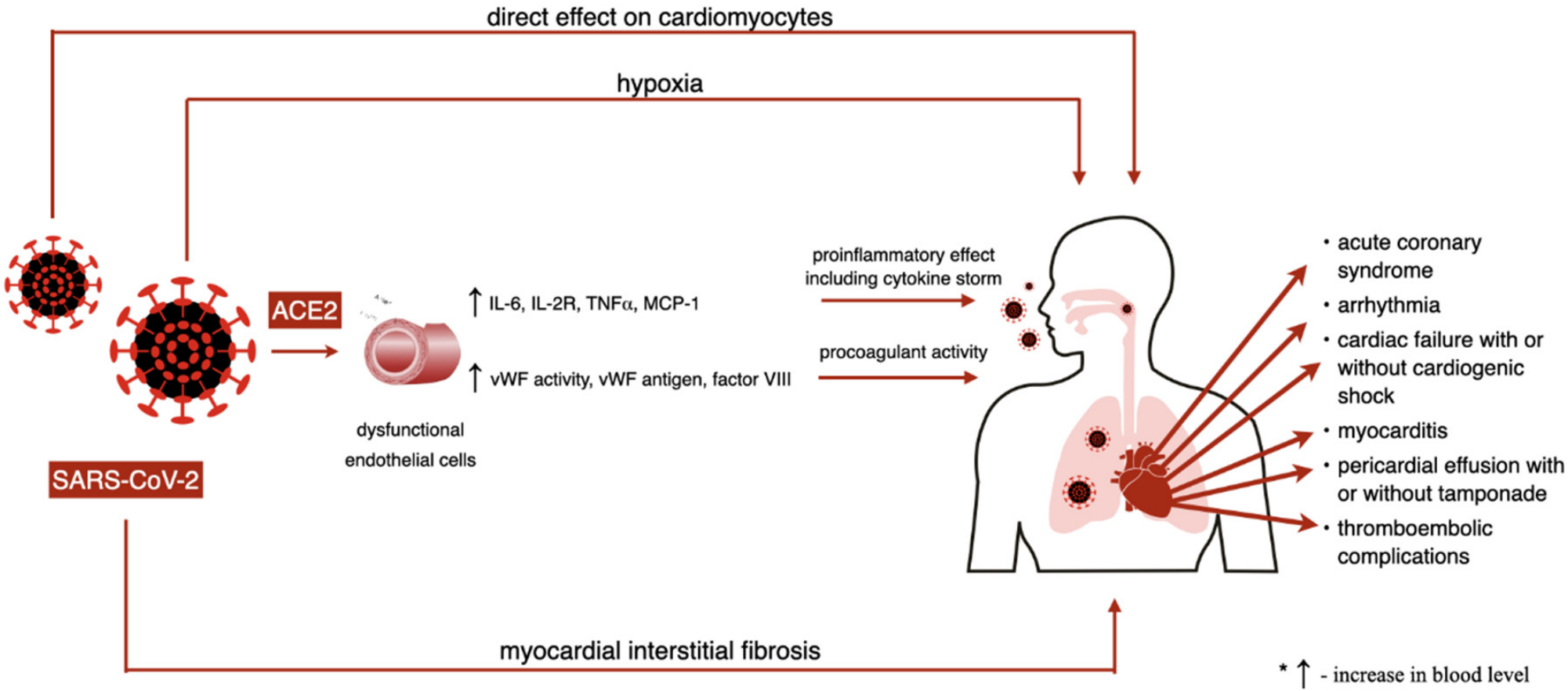
CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Sản phẩm ly giải huyết khối: D-dimer và FDPs

Richard C. Becker, Journal of Thrombosis and Thrombolysis (2020) 50:54–67

CƠ CHẾ SINH HUYẾT KHỐI Ở BỆNH NHÂN COVID-19



Cơ chế gây huyết khối trên mạch vành của SARS-CoV2

Oliwia Grzegorowska *J. Clin. Med.* **2020**, *9*, 3746

BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG

	All patients (n=41)	ICU care (n=13)	No ICU care (n=28)	p value
White blood cell count, $\times 10^9$ per L	6·2 (4·1–10·5)	11·3 (5·8–12·1)	5·7 (3·1–7·6)	0·011
<4	10/40 (25%)	1/13 (8%)	9/27 (33%)	0·041
4–10	18/40 (45%)	5/13 (38%)	13/27 (48%)	..
>10	12/40 (30%)	7/13 (54%)	5/27 (19%)	..
Neutrophil count, $\times 10^9$ per L	5·0 (3·3–8·9)	10·6 (5·0–11·8)	4·4 (2·0–6·1)	0·00069
Lymphocyte count, $\times 10^9$ per L	0·8 (0·6–1·1)	0·4 (0·2–0·8)	1·0 (0·7–1·1)	0·0041
<1·0	26/41 (63%)	11/13 (85%)	15/28 (54%)	0·045
≥1·0	15/41 (37%)	2/13 (15%)	13/28 (46%)	..
Haemoglobin, g/L	126·0 (118·0–140·0)	122·0 (111·0–128·0)	130·5 (120·0–140·0)	0·20
Platelet count, $\times 10^9$ per L	164·5 (131·5–263·0)	196·0 (165·0–263·0)	149·0 (131·0–263·0)	0·45
<100	2/40 (5%)	1/13 (8%)	1/27 (4%)	0·45
≥100	38/40 (95%)	12/13 (92%)	26/27 (96%)	..
Prothrombin time, s	11·1 (10·1–12·4)	12·2 (11·2–13·4)	10·7 (9·8–12·1)	0·012
Activated partial thromboplastin time, s	27·0 (24·2–34·1)	26·2 (22·5–33·9)	27·7 (24·8–34·1)	0·57
D-dimer, mg/L	0·5 (0·3–1·3)	2·4 (0·6–14·4)	0·5 (0·3–0·8)	0·0042

Báo cáo đầu tiên từ Vũ Hán, Trung Quốc về đặc điểm lâm sàng của COVID-19

Chaolin Huang, ***Lancet*** **2020; 395: 497–506**

BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG

Parameters	Normal range	Total (n = 183)	Survivors (n = 162)	Non-survivors (n = 21)	*P* values
Age (years)		54.1 ± 16.2	52.4 ± 15.6	64.0 ± 20.7	<.001
Sex (male/female)		98/85	82/80	16/5	.035
With underlying diseases		75 (41.0%)	63 (38.9%)	12 (57.1%)	.156
On admission					
PT (sec)	11.5-14.5	13.7 (13.1-14.6)	13.6 (13.0-14.3)	15.5 (14.4-16.3)	<.001
APTT (sec)	29.0-42.0	41.6 (36.9-44.5)	41.2 (36.9-44.0)	44.8 (40.2-51.0)	.096
Fibrinogen (g/L)	2.0-4.0	4.55 (3.66-5.17)	4.51 (3.65-5.09)	5.16 (3.74-5.69)	.149
D-dimer (μg/mL)	<0.50	0.66 (0.38-1.50)	0.61 (0.35-1.29)	2.12 (0.77-5.27)	<.001
FDP (μg/mL)	<5.0	4.0 (4.0-4.9)	4.0 (4.0-4.3)	7.6 (4.0-23.4)	<.001
AT (%)	80-120	91 (83-97)	91 (84-97)	84 (78-90)	.096

Bất thường đông máu trên bệnh nhân COVID-19 tại Vũ Hán, Trung Quốc

Ning Tang, *J Thromb Haemost.* 2020;18:844–847

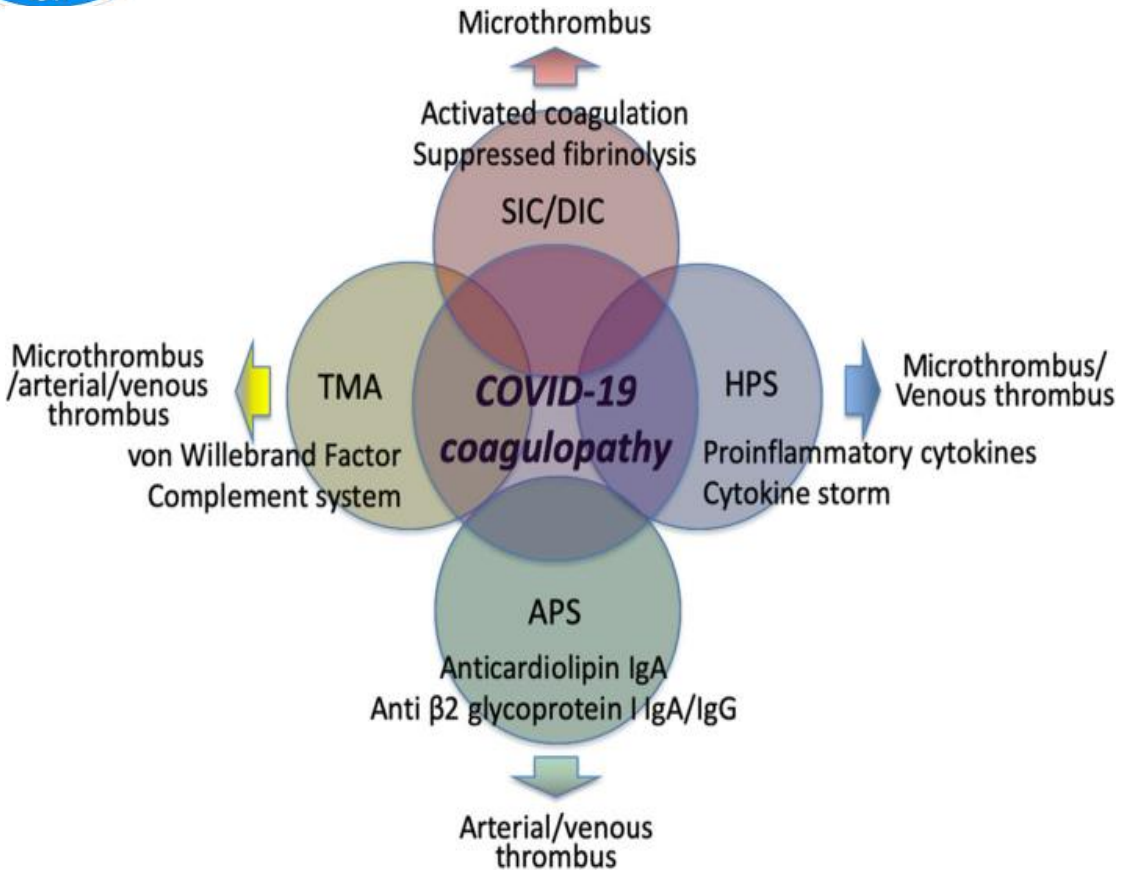
TABLE 2 The grade of DIC in non-survivors with NCP (n = 21)

	Number of patients (%)
Platelet counts ($\times 10^9$/L)	
50-100 (1 point)	7 (33.3)
<50 (2 points)	5 (23.8)
D-dimer (μg/mL)	
1.0-3.0 (2 points)	3 (14.3)
>3.0 (3 points)	18 (85.7)
Fibrinogen (g/L)	
<1.0 (1 point)	6 (28.6)
Prolongation of PT (sec)	
3-6 (1 point)	5 (23.8)
>6 (2 points)	10 (47.6)
Meeting the ISTH criteria of DIC (Total points ≥5)	15 (71.4)

Tỉ lệ bệnh nhân SARS-CoV2 đối chiếu với tiêu chuẩn DIC của ISTH

Ning Tang, *J Thromb Haemost.* 2020;18:844–847

BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG



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

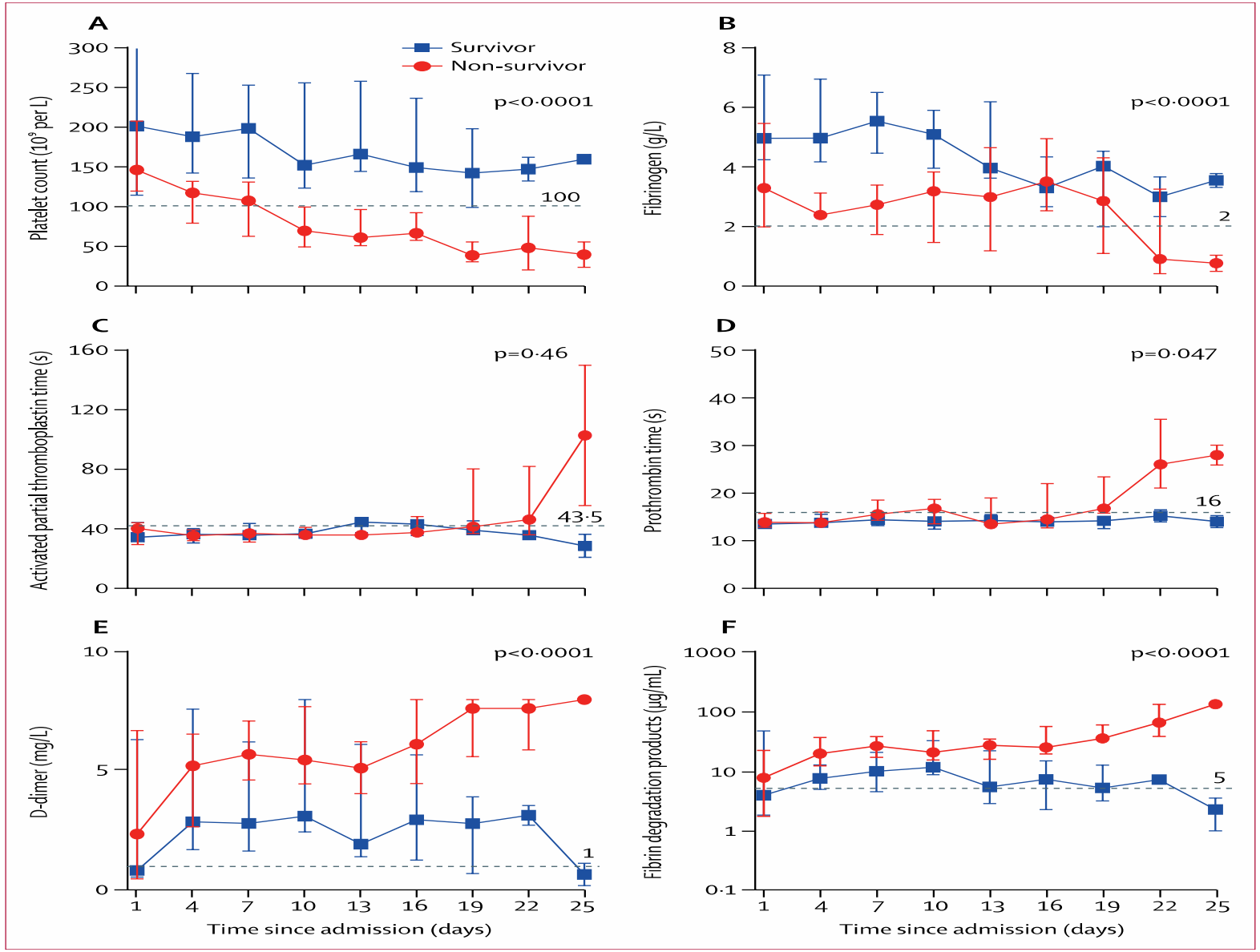
Bệnh lý đông máu do COVID-19 chia sẻ các đặc điểm lâm sàng của các bệnh lý đông máu khác

Richard C. Becker, Journal of Thrombosis and Thrombolysis (2020) 50:54–67
Iba et al. Critical Care (2020) 24:360

	Missing data	Total (n=380)	Moderate disease (n=149)	Severe disease (n=145)	Critical disease (n=86)	p value			
						Overall	Moderate vs Severe	Moderate vs Critical	Severe vs Critical
Platelet count, 10^9 cells per L	0	189·50 (121·50–271·00)	198·00 (145·50–249·50)	227·00 (142·50–328·00)	105·00 (55·75–200·75)	<0·0001	0·23	<0·0001	<0·0001
<100	..	71/380 (19%)	9/149 (6%)	20/145 (14%)	42/86 (49%)	<0·0001*	0·077	<0·0001	<0·0001
≥100	..	309/380 (81%)	140/149 (94%)	125/145 (86%)	44/86 (51%)	..	..	..	..
Activated partial thromboplastin time, s	30	37·40 (34·30–42·33)	36·20 (33·38–39·70)	37·60 (35·13–42·48)	38·80 (34·23–48·15)	0·0018	0·028	0·0021	0·85
≤43·5	..	274/350 (78%)	116/130 (89%)	106/136 (78%)	52/84 (62%)	<0·0001*	0·040	<0·0001	0·031
>43·5	..	76/350 (22%)	14/130 (11%)	30/136 (22%)	32/84 (38%)	..	..	..	..
Prothrombin time, s	31	13·60 (12·80–14·80)	13·00 (12·50–13·70)	13·70 (12·90–14·55)	16·60 (14·00–21·98)	<0·0001	<0·0001	<0·0001	<0·0001
Fibrinogen, g/L	75	4·37 (3·39–5·46)	4·29 (3·42–5·23)	4·80 (3·62–5·96)	3·96 (2·60–5·14)	0·00064	0·044	0·34	0·0014
<2	..	18/305 (6%)	1/135 (1%)	0/86	17/84 (20%)	<0·0001†	1·0	<0·0001	<0·0001
≥2	..	287/305 (94%)	134/135 (99%)	86/86 (100%)	67/84 (80%)	..	..	..	..
D-dimer, mg/L	47	1·24 (0·47–4·58)	0·42 (0·22–0·91)	1·36 (0·65–3·06)	7·24 (3·39–8·00)	<0·0001	<0·0001	<0·0001	<0·0001
Fibrin degradation products, µg/mL	132	3·20 (1·70–10·98)	1·90 (1·23–3·18)	4·20 (2·10–11·60)	28·20 (6·00–113·15)	<0·0001*	<0·0001	<0·0001	<0·0001
Antithrombin III activity, %	132	90·00 (79·00–97·00)	92·00 (84·00–98·75)	88·00 (78·00–95·00)	85·00 (70·25–97·50)	0·014	0·028	0·086	1·0
<80	..	66/248 (27%)	17/108 (16%)	33/95 (35%)	16/45 (36%)	0·0030*	0·0052	0·020	1·0
≥80	..	182/248 (73%)	91/108 (84%)	62/95 (65%)	29/45 (64%)	..	..	..	..

Sự thay đổi các chỉ số đông máu và mức độ nặng của bệnh

Danying L., 2020, Lancet Hematol



Sự thay đổi của các marker đông máu trên 12 bệnh nhân sống và 8 bệnh nhân tử vong

Danying L., 2020, Lancet Hematol

	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value
Demographics and clinical characteristics				
Age, years*	1·14 (1·09–1·18)	<0·0001	1·10 (1·03–1·17)	0·0043
Female sex (*vs* male)	0·61 (0·31–1·20)	0·15	..	..
Current smoker (*vs* non-smoker)	2·23 (0·65–7·63)	0·20	..	..
Comorbidity present (*vs* not present)				
Chronic obstructive lung disease	5·40 (0·96–30·40)	0·056	..	..
Coronary heart disease	21·40 (4·64–98·76)	<0·0001	2·14 (0·26–17·79)	0·48
Diabetes	2·85 (1·35–6·05)	0·0062	..	..
Hypertension	3·05 (1·57–5·92)	0·0010	..	..
Respiratory rate, breaths per min				
≤24	1 (ref)	..	..	..
>24	8·89 (4·34–18·19)	<0·0001	..	..
SOFA score	6·14 (3·48–10·85)	<0·0001	5·65 (2·61–12·23)	<0·0001
qSOFA score	12·00 (5·06–28·43)	<0·0001	..	..
Laboratory findings				
White blood cell count, × 10^9 per L				
<4	0·73 (0·26–2·10)	0·56	..	..
4–10	1 (ref)	..	..	..
>10	6·60 (3·02–14·41)	<0·0001	..	..
Lymphocyte count, × 10^9 per L*	0·02 (0·01–0·08)	<0·0001	0·19 (0·02–1·62)	0·13
ALT, U/L				
≤40	1 (ref)	..	..	..
>40	2·87 (1·48–5·57)	0·0018	..	..

(Table 3 continues in next column)

(Continued from previous column)

	Univariable OR (95% CI)	p value	Multivariable OR (95% CI)	p value
Creatinine, µmol/L				
≤133	1 (ref)	..	..	..
>133	4·39 (1·01–19·06)	0·048	..	..
Lactate dehydrogenase, U/L				
≤245	1 (ref)	..	..	..
>245	45·43 (6·10–338·44)	0·0002	..	..
Creatine kinase, U/L				
≤185	1 (ref)	..	..	..
>185	2·56 (1·03–6·36)	0·043	..	..
High-sensitivity cardiac troponin I, pg/mL				
≤28	1 (ref)	..	..	..
>28	80·07 (10·34–620·36)	<0·0001	..	..
D-dimer, µg/mL				
≤0·5	1 (ref)	..	1 (ref)	..
> 0·5	1·96 (0·52–7·43)	0·32	2·14 (0·21–21·39)	0·52
> 1	20·04 (6·52–61·56)	<0·0001	18·42 (2·64–128·55)	0·0033
Prothrombin time, s				
<16	1 (ref)	..	..	..
≥16	4·62 (1·29–16·50)	0·019	..	..
Serum ferritin, µg/L				
≤300	1 (ref)	..	..	..
>300	9·10 (2·04–40·58)	0·0038	..	..
IL-6, pg/mL*	1·12 (1·03–1·23)	0·0080	..	..
Procalcitonin, ng/mL*	13·75 (1·81–104·40)	0·011	..	..

OR=odds ratio. SOFA=Sequential Organ Failure Assessment. qSOFA=Quick SOFA. ALT=alanine aminotransferase. IL-6=interleukin-6. *Per 1 unit increase.

Table 3: **Risk factors associated with in-hospital death**

Các yếu tố nguy cơ tử vong trên bệnh nhân SARS-CoV2

Fei Z., 2020, The Lancet

BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG

Characteristics	Normal range	VTE (n = 20)	Non-VTE (n = 61)	*P*-value
Age (years)	-	68.4 ± 9.1	57.1 ± 14.3	<.001
Leucocytes ($\times 10^9$/L)	3.5-9.5	7.8 ± 3.1	6.6 ± 2.6	.120
Lymphocytes ($\times 10^9$/L)	1.1-3.2	0.8 ± 0.4	1.3 ± 0.6	<.001
Platelets ($\times 10^9$/L)	125.0-350.0	246.6 ± 110.6	248.8 ± 111.7	.938
Haemoglobin (g/L)	115.0-150.0	123.2 ± 16.5	125.3 ± 16.7	.633
APTT (s)	27.0-45.0	39.9 ± 6.4	35.6 ± 4.5	.001
Prothrombin time (s)	11.0-16.0	15.4 ± 1.0	15.6 ± 1.0	.465
D-dimer (µg/mL)	0.0-0.5	5.2 ± 3.0	0.8 ± 1.2	<.001

Xuất độ VTE là 25% tại ICU, bệnh viện Thống Nhất Vũ Hán, Trung Quốc

Sonping C., 2020, International Society on Thrombosis and Haemostasis

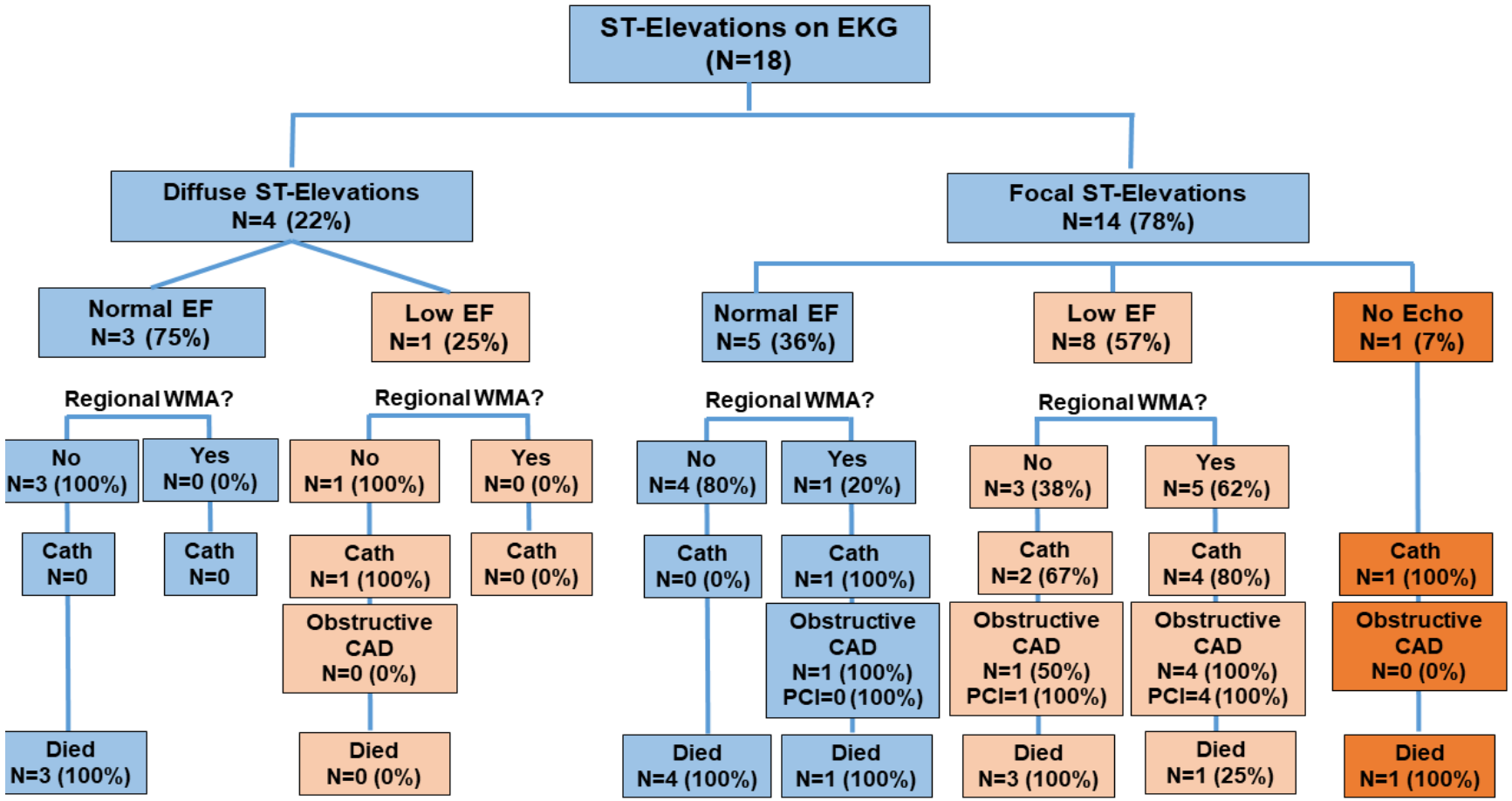
TABLE 3 Sensitivity, specificity, PPV, and NPV of different D-dimer cut-off levels for predicting VTE in NCP patients

Cut-off (µg/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
1.0	85.0	77.0	54.8	94.0
1.5	85.0	88.5	70.8	94.7
2.0	80.0	90.2	72.7	93.2
2.5	70.0	93.4	77.8	90.5
3.0	70.0	96.7	87.5	90.8
3.5	65.0	96.7	86.7	89.4

Cut-off D-dimer trong tiên đoán huyết khối tĩnh mạch sâu

Sonping C., 2020, International Society on Thrombosis and Haemostasis

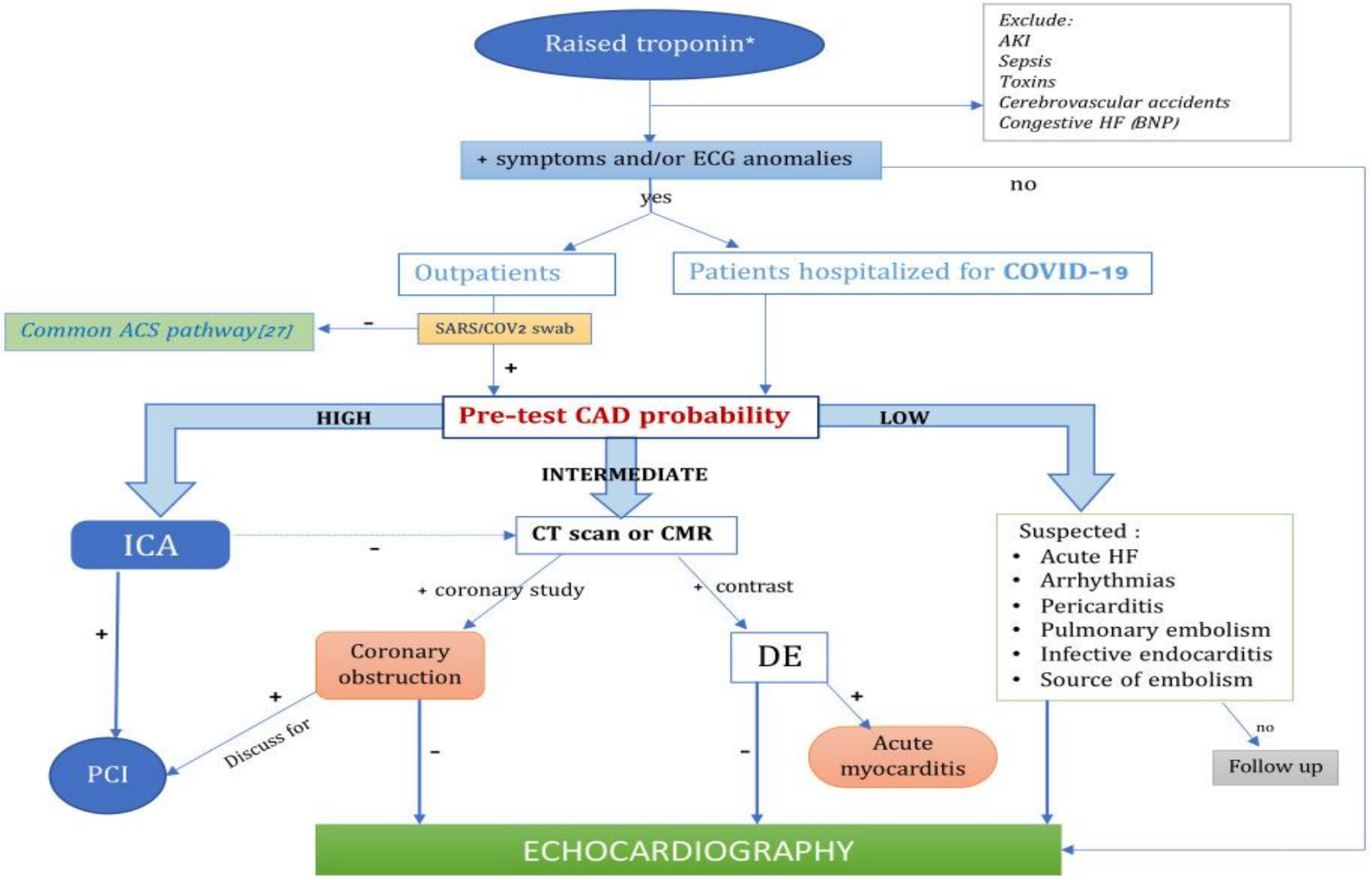
BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG



Báo cáo loạt ca hội chứng vành cấp trên bệnh nhân COVID-19

Sripal Bangalore N Engl J Med 2020; 382:2478-2480

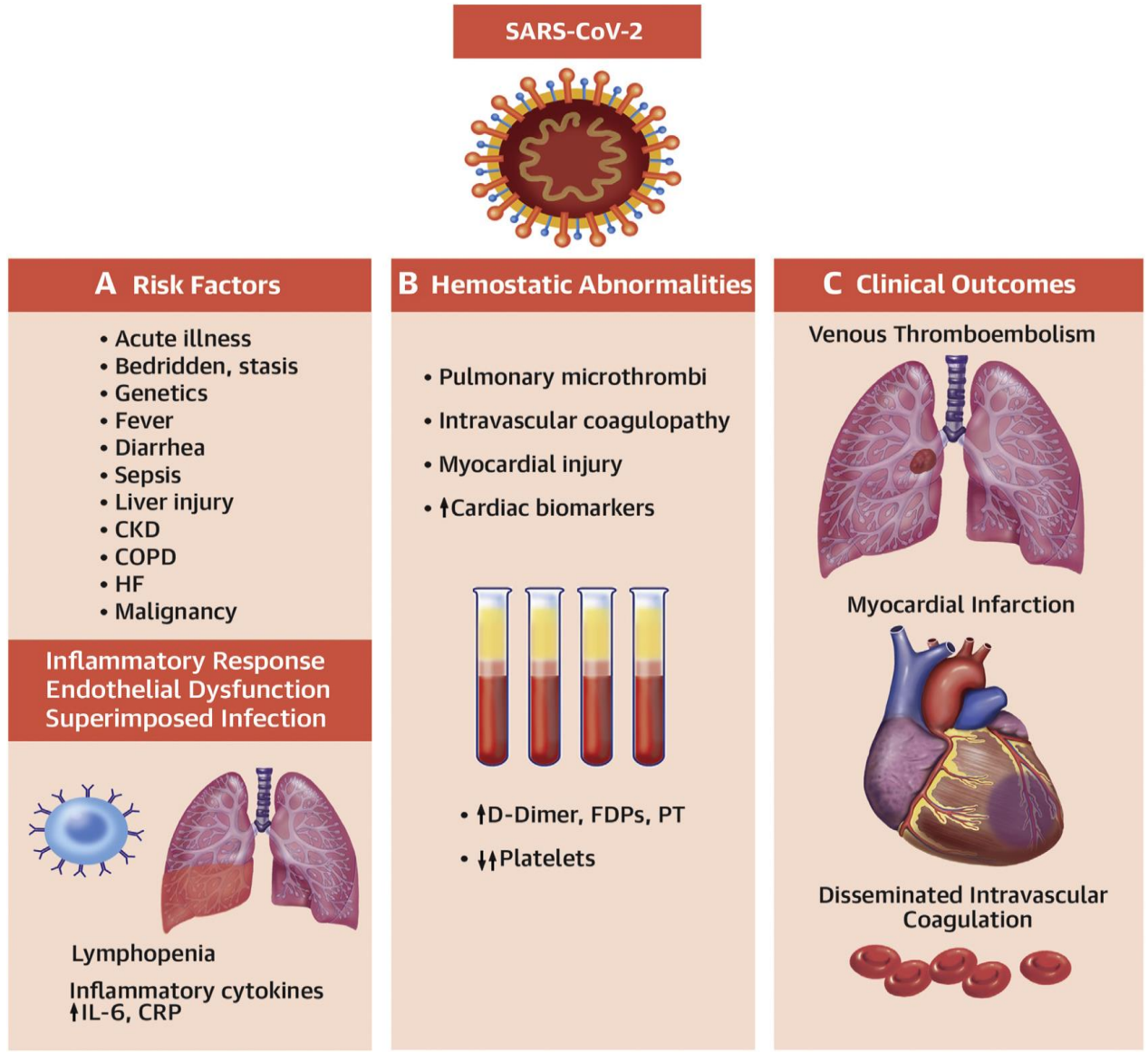
BIỂU HIỆN LÂM SÀNG VÀ CẬN LÂM SÀNG



Lưu đồ tiếp cận tăng men tim trên bệnh nhân SARS-CoV 2

Matteo Cameli, Front. Cardiovasc. Med., 28 January 2021

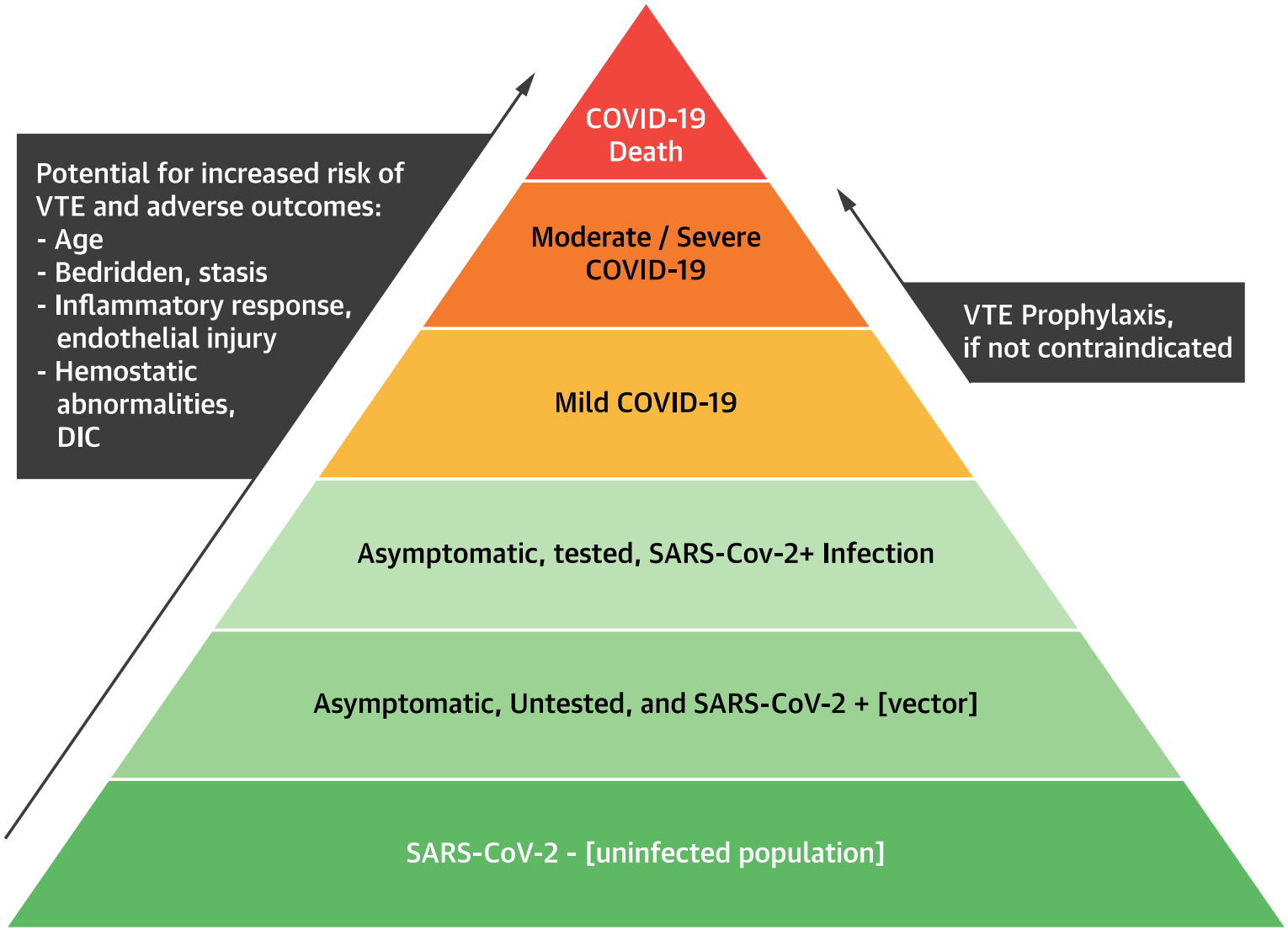
CENTRAL ILLUSTRATION Postulated Mechanisms of Coagulopathy and Pathogenesis of Thrombosis in COVID-19



Bikdeli, B. et al. J Am Coll Cardiol. 2020;75(23):2950-73.

JBikdeli et al. ACC VOL. 75, NO. 23, 2020

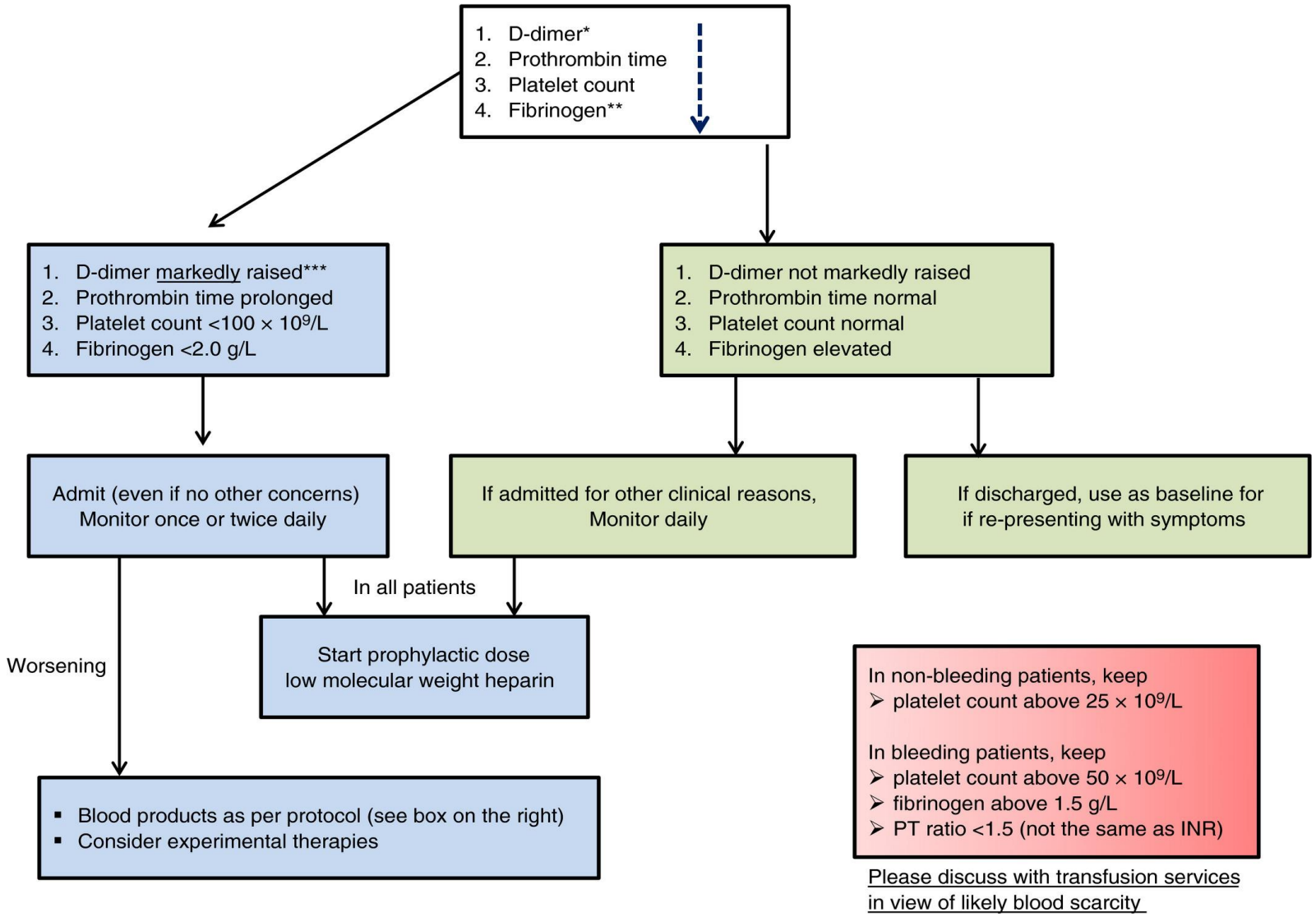
CÁC KHUYẾN CÁO VỀ ĐIỀU TRỊ CHỐNG HUYẾT KHỐI



Nguy cơ huyết khối và mức độ nặng của bệnh

JBikdeli et al. ACC VOL. 75, NO. 23, 2020

Hướng dẫn chẩn đoán và xử trí bệnh lý đông máu do SARS-CoV2 của ISTH



Journal of Thrombosis and Haemostasis, 2020, Volume: 18, Issue: 5, Pages: 1023-1026,

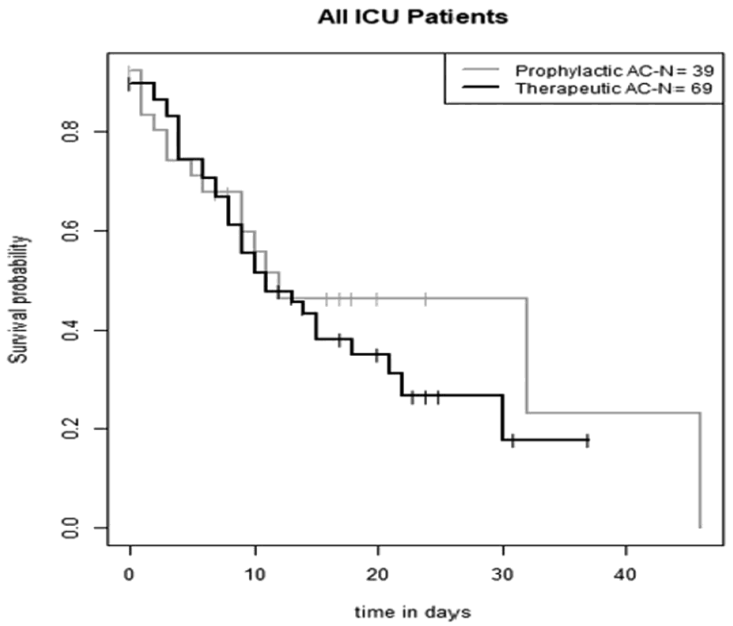
Cần thiết tăng liều kháng đông dự phòng trên bệnh nhân SARS-CoV 2 nặng?

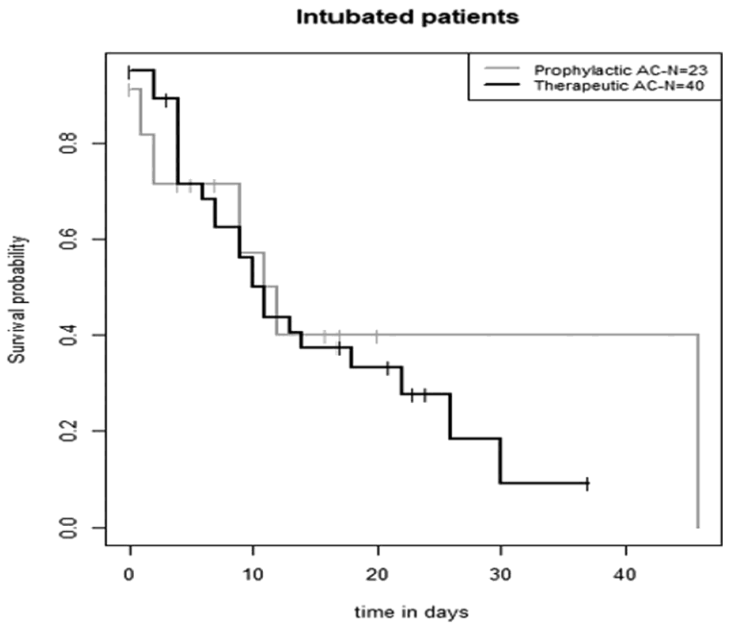
	Study period		
	2019, February 27th to March 31th (all ICU patients*, n=196)	**2019**, 1st January to 31th December (Influenza ICU patients (PCR+), n=40)	**2020**, February 27th to March 31th (COVID-19 ICU patients, (PCR+), n=107)
Number of chest CT scans, n (%)	50 (25.5)	20 (50.0)	36 (33.6)
Number of CTPA, n (%)	30 (15.3)	17 (42.5)	34 (31.8)
Number of CTPA performed for a PE diagnosis, n (%)	20 (10.2)	8 (20.0)	34 (31.8)
Number of PE cases (%)	12 (6.1)	3 (7.5)	22 (20.6)**
Bilateral, n (%)	8 (66.6)	0***	8 (40.0)§
Proximal, n (%)	2 (16.6)	0***	2 (10.0)§
Segmental, n (%)	6 (50.0)	0***	11 (55.0)§
ARDS, n (%)	14 (7.1)	15 (37.5)	67 (62.6)
Intubation, n (%)	84 (42.9)	17 (42.5)	67 (62.6)
Doppler ultrasound, n (%)	12 (6.1)	2 (5.0)	8 (7.5)
DVT, n (%)	9 (4.6)	1 (2.5)	5 (4.7)

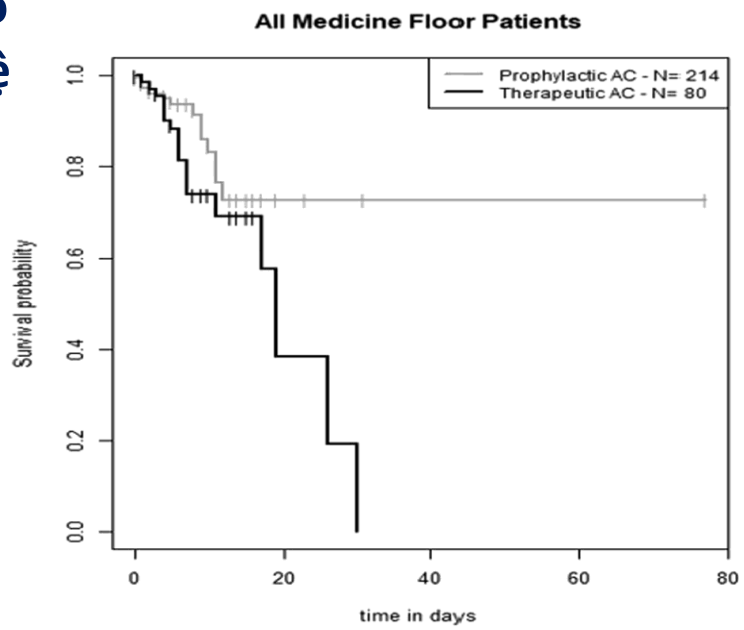
Tỉ lệ thuyên tắc phổi ở nhóm nhiễm SARS-CoV 2 cao hơn so với bệnh nhân ICU khác và bệnh nhân mắc cúm

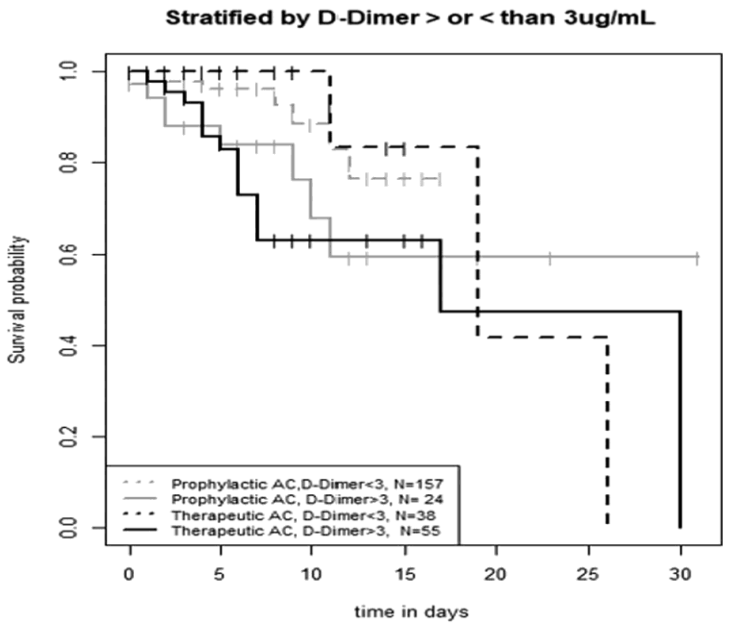
Poissy et al 10.1161/CIRCULATIONAHA.120.047430

Kháng đông liều điều trị theo kinh nghiệm không cải thiện tỉ lệ tử vong





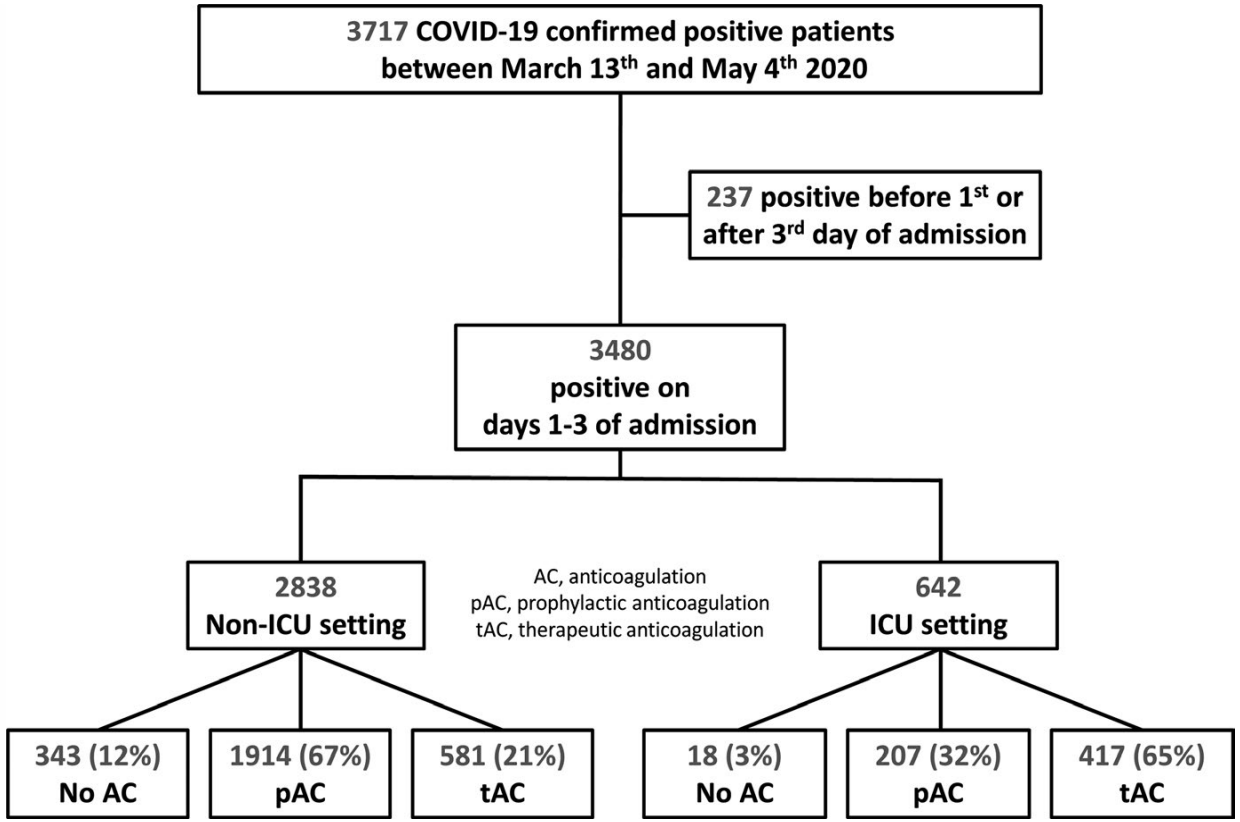




Thrombosis Research 197 (2021) 65–68

Liều kháng đông điều trị hay dự phòng trên bệnh nhân SARS-CoV 2 ?

HỒI CỨU ĐA TRUNG TÂM TẠI 8 BỆNH VIỆN VÙNG NAM MICHIGAN

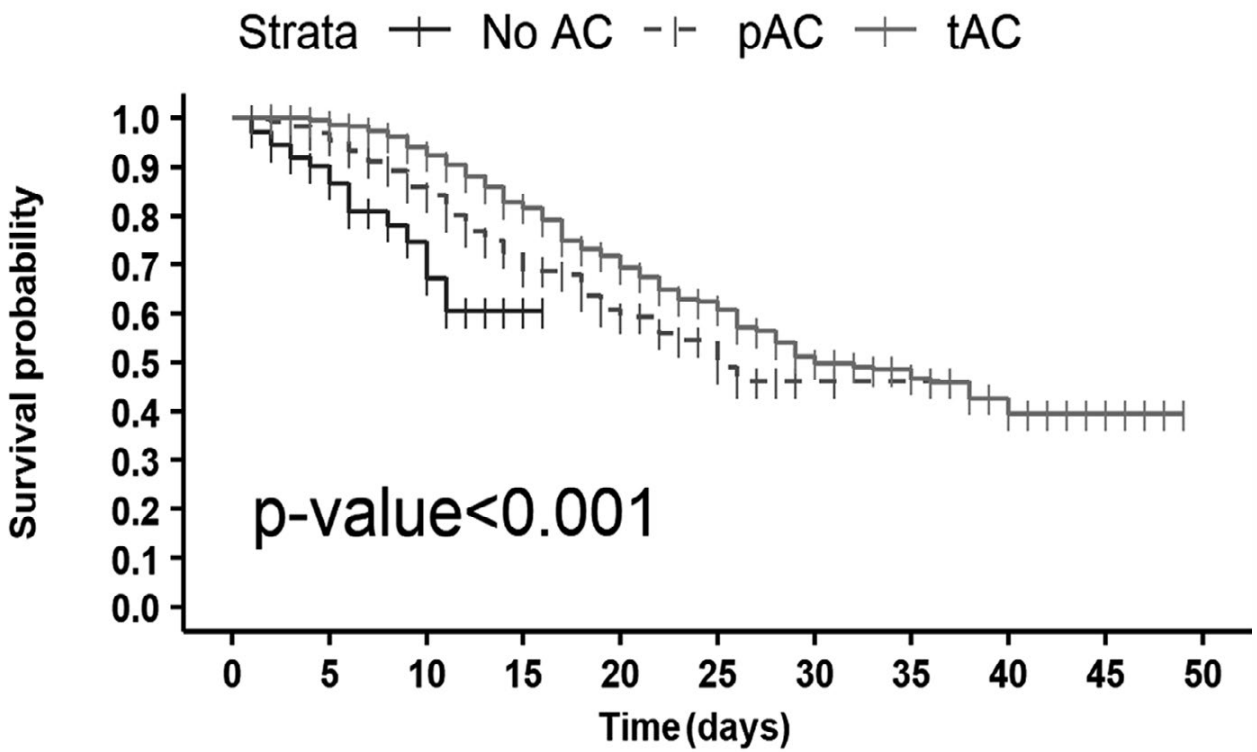


❖ Chỉ định kháng đông điều trị:
- Bệnh nhân thở máy
- Suy thận diễn tiến
- D-dimer > 3000 ng/mL
- Theo kinh nghiệm bác sĩ lâm sàng

❖ Chiến lược
- UFH truyền liên tục (aPTT >45s)
- Enoxaparin 1 mg/kg x 2 hoặc 1.5 mg/kg (TDD) dựa trên chức năng thận
- Agatroban truyền liên tục
- Fondaparinux 5-10 mg (TDD) dựa trên cân nặng
- Kháng đông uống

Filip I. , Eur J Haematol. 2021;106:165–174.

Liều kháng đông điều trị hay dự phòng trên bệnh nhân SARS-CoV 2 ?



	Hazard ratio	Confidence interval	Significance
Age (years)	1.6 [a]	1.4-1.8	<.001
BMI (kg/m^2)[b]			
<18.5 kg/m^2	3.0	1.5-6.0	.001
30-40 kg/m^2	0.8	0.6-1.1	.214
≥40 kg/m^2	1.1	0.7-1.6	.779
ICU stay	5.2	3.5-7.8	<.001
Prophylactic anticoagulation[c]	0.35	0.22-0.54	<.001
Therapeutic anticoagulation[c]	0.14	0.08-0.23	<.001
AKI requiring dialysis	1.3	0.96-1.8	.095
HQ and Azithromycin			
HQ	0.7	0.4-1.2	.29
Azithromycin	1.4	0.6-3.1	.41
HQ and Azithromycin	0.7	0.4-1.2	.27

Tăng liều kháng đông có thể cải thiện khả năng sống còn

Filip I. , Eur J Haematol. 2021;106:165–174.

BIẾN CHỨNG XUẤT HUYẾT DO THUỐC KHÁNG ĐÔNG

	All patients (n = 3480)	No AC (n = 361)	pAC (n = 2121)	tAC (n = 998)	Significance
Major bleeding	147 (4.2%)	20 (5.5%)	46 (2.2%)	81 (8.1%)	**<.001**
No major bleeding	3333 (95.8%)	341 (94.5%)	2075 (97.8%)	917 (91.9%)	
≥5 units PRBC in 48 h	70 (2.0%)	9 (2.5%)	18 (0.9%)	43 (4.3%)	**<.001**
<5 units PRBC in 48 h	3410 (98.0%)	352 (97.5%)	2103 (99.1%)	955 (95.7%)	
Intracranial hemorrhage	27 (0.8%)	4 (1.1%)	10 (0.5%)	13 (1.3%)	**.028**
No intracranial hemorrhage	3453 (99.2%)	357 (98.9%)	2111 (99.5%)	985 (98.7%)	
Severe thrombocytopenia	71 (0.2%)	10 (2.8%)	27 (1.3%)	34 (3.4%)	**<.001**
No severe thrombocytopenia	3406 (97.8%)	349 (97.2%)	2093 (98.7%)	964 (96.6%)	

Filip I. , Eur J Haematol. 2021;106:165–174.

blood
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Washington, DC 20036
Phone: 202-776-0544 | Fax 202-776-0545
editorial@hematology.org

CHIẾN LƯỢC SỬ DỤNG KHÁNG ĐÔNG THEO PHÂN LOẠI BỆNH NHÂN

COVID-19 and its implications for thrombosis and anticoagulation

Tracking no: BLD-2020-006000-CR2

Jean Connors (Harvard Medical School, United States) Jerrold Levy (Duke University School of Medicine, United States)

COVID-19 positive	Coagulation tests	Standard dose VTE prophylaxis	Escalated[1] dose VTE prophylaxis	Therapeutic dose anticoagulation
Outpatient		**Consider**[2]		
Inpatient	**X**			
Ward	**X**	**X**		
ICU	**X**		**X**	
Confirmed VTE	**X**			**X**
Presumed PE[3]	**X**			**X**
ARDS	**X**		**X**	

KHUYẾN CÁO CỦA HỘI TIM MẠCH HOA KỲ ĐỐI VỚI VTE VÀ ACS TRÊN BỆNH NHÂN COVID-19

HIGH-RISK COVID-19†

LOW/INTERMEDIATE RISK ACS OR VTE

For ACS:
- GDMT per ACS algorithm
- Other therapies reserved for select cases such as those with significant recurrent/persistent symptoms or decompensation

For VTE:
- Anticoagulant therapy
- Other therapies reserved for select cases such as those with significant recurrent/persistent symptoms or decompensation

Nguy cơ trung bình/ thấp

HIGH-RISK ACS OR VTE*

For ACS:
- GDMT per ACS algorithm
- Consider emergent TTE
- Urgent/emergent angiography and intervention vs. systemic fibrinolysis
- Consider need and safety of hemodynamic support and monitoring in select patients

For VTE:
- Anticoagulant therapy
- Consider systemic fibrinolysis
- Catheter-directed or surgical therapies in case not suitable for systemic fibrinolysis
- Consider need and safety of hemodynamic support and monitoring

Nguy cơ cao ACS/ VTE

JBikdeli et al. ACC VOL. 75, NO. 23, 2020

KHUYẾN CÁO CỦA HỘI TIM MẠCH HOA KỲ ĐỐI VỚI VTE VÀ ACS TRÊN BỆNH NHÂN COVID-19

TABLE 6 Summary of Consensus Recommendation on Antithrombotic Therapy During the COVID-19 Pandemic

Patients with mild COVID-19 (outpatient)

For outpatients with mild COVID-19, increased mobility should be encouraged. Although indiscriminate use of pharmacological VTE prophylaxis should not be pursued, assessment for the risk of VTE and of bleeding is reasonable. Pharmacologic prophylaxis could be considered after risk assessment on an individual case basis for patients who have elevated risk VTE, without high bleeding risk.*

There is no known risk of developing severe COVD-19 due to taking antithrombotic agents (i.e., antiplatelet agents or anticoagulants). If patients have been taking antithrombotic agents for prior known thrombotic disease, they should continue their antithrombotic agents as recommended.

For outpatients on vitamin K antagonists who do not have recent stable INRs, and are unable to undergo home or drive-through INR testing, it is reasonable to transition the treatment DOACs if there are no contraindications and no problems with drug availability and affordability. If DOACs are not approved or available, LMWH can be considered as alternative.*

Patients with moderate or severe COVID-19 without DIC (hospitalized)

Hospitalized patients with COVID-19 should undergo risk stratification for VTE prophylaxis.

For hospitalized patients with COVID-19 and not in DIC, prophylactic doses of anticoagulation should be administered to prevent VTE.*†‡ If pharmacological prophylaxis is contraindicated, it is reasonable to consider intermittent pneumatic compression.

For hospitalized patients with COVID-19 and not in DIC, there are insufficient data to consider routine therapeutic or intermediate-dose parenteral anticoagulation with UFH or LMWH.*§

Routine screening for VTE (e.g., bilateral lower extremity ultrasound) for hospitalized patients with COVID-19 with elevated D-dimer (>1,500 ng/ml) cannot be recommended at this point.||

Nhóm bệnh nhân không có DIC

JBikdeli et al. ACC VOL. 75, NO. 23, 2020

KHUYẾN CÁO CỦA HỘI TIM MẠCH HOA KỲ ĐỐI VỚI VTE VÀ ACS TRÊN BỆNH NHÂN COVID-19

Patients with moderate or severe COVID-19 and suspected or confirmed DIC (hospitalized)

For patients with moderate or severe COVID-19 and in DIC but without overt bleeding, prophylactic anticoagulation should be administered.*†¶

For hospitalized patients with COVID-19 with suspected or confirmed DIC, but no overt bleeding, there are insufficient data to consider routine therapeutic or intermediate-dose parenteral anticoagulation with UFH or LMWH.*

For patients with moderate or severe COVID-19 on chronic therapeutic anticoagulation, who develop suspected or confirmed DIC without overt bleeding, it is reasonable to consider the indication for anticoagulation and weigh with risk of bleeding when making clinical decisions regarding dose adjustments or discontinuation. The majority of authors of this paper recommended reducing the intensity of anticoagulation in this clinical circumstance, unless the risk of thrombosis is considered to be exceedingly high.#

For patients with moderate or severe COVID-19 and an indication for dual antiplatelet therapy (e.g., percutaneous coronary intervention within the past 3 months or recent myocardial infarction) and with suspected or confirmed DIC without overt bleeding, in the absence of evidence, decisions for antiplatelet therapy need to be individualized. In general, it is reasonable to continue dual antiplatelet therapy if platelet count is >50,000, reduce to single antiplatelet therapy if platelet count is >25,000 and <50,000, and discontinue if platelet count is <25,000. However, these guidelines may be revised upward or downward depending on the individualized relative risk of thrombotic complications vs. bleeding.

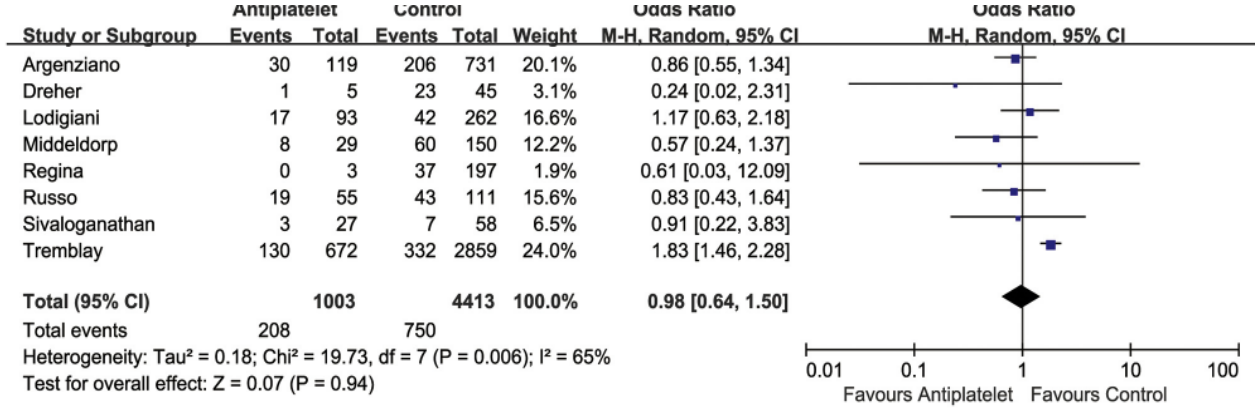
For patients who were admitted and are now being discharged for COVID-19, routine screening for VTE risk is reasonable for consideration of pharmacological prophylaxis for up to 45 days post-discharge. Pharmacological prophylaxis should be considered if there is elevated risk for thrombotic events, without high bleeding risk.**

Ambulation and physical activity should be encouraged.

Nhóm bệnh nhân có DIC

JBikdeli et al. ACC VOL. 75, NO. 23, 2020

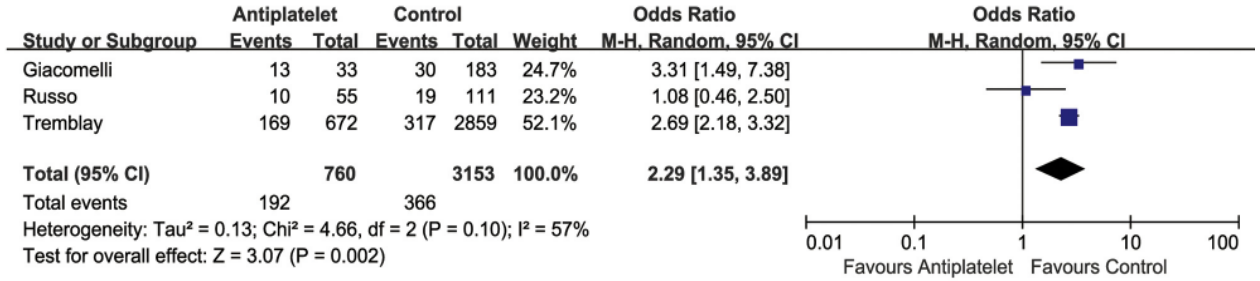
VAI TRÒ CỦA CÁC THUỐC KHÁNG KẾT TẬP TIỂU CẦU TRÊN BỆNH NHÂN COVID-19



Study or Subgroup	Antiplatelet Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Argenziano	30	119	206	731	20.1%	0.86 [0.55, 1.34]
Dreher	1	5	23	45	3.1%	0.24 [0.02, 2.31]
Lodigiani	17	93	42	262	16.6%	1.17 [0.63, 2.18]
Middeldorp	8	29	60	150	12.2%	0.57 [0.24, 1.37]
Regina	0	3	37	197	1.9%	0.61 [0.03, 12.09]
Russo	19	55	43	111	15.6%	0.83 [0.43, 1.64]
Sivaloganathan	3	27	7	58	6.5%	0.91 [0.22, 3.83]
Tremblay	130	672	332	2859	24.0%	1.83 [1.46, 2.28]
Total (95% CI)		**1003**		**4413**	**100.0%**	**0.98 [0.64, 1.50]**
Total events	208		750			

Heterogeneity: Tau² = 0.18; Chi² = 19.73, df = 7 (P = 0.006); I² = 65%
Test for overall effect: Z = 0.07 (P = 0.94)

Figure 1B



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Russo	10	55	19	111	23.2%	1.08 [0.46, 2.50]
Tremblay	169	672	317	2859	52.1%	2.69 [2.18, 3.32]
Total (95% CI)		**760**		**3153**	**100.0%**	**2.29 [1.35, 3.89]**
Total events	192		366			

Heterogeneity: Tau² = 0.13; Chi² = 4.66, df = 2 (P = 0.10); I² = 57%
Test for overall effect: Z = 3.07 (P = 0.002)

Figure 1C

Figure 1A

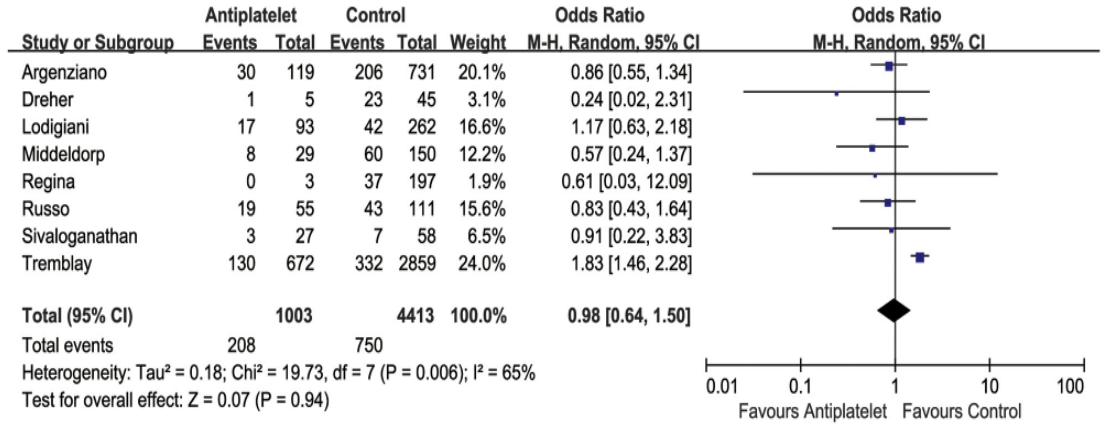

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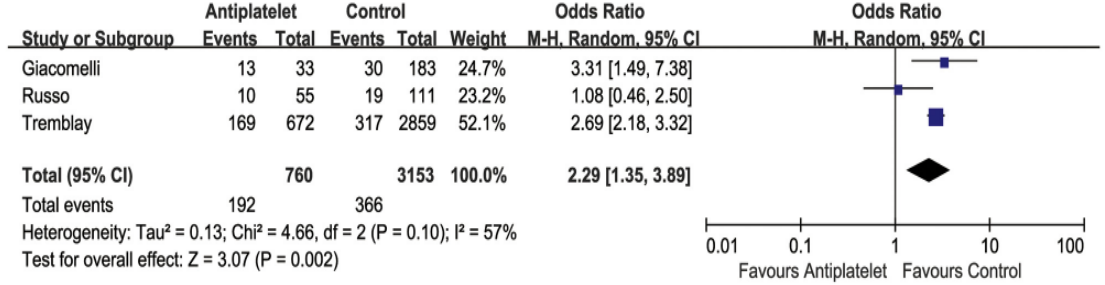
Figure 1B



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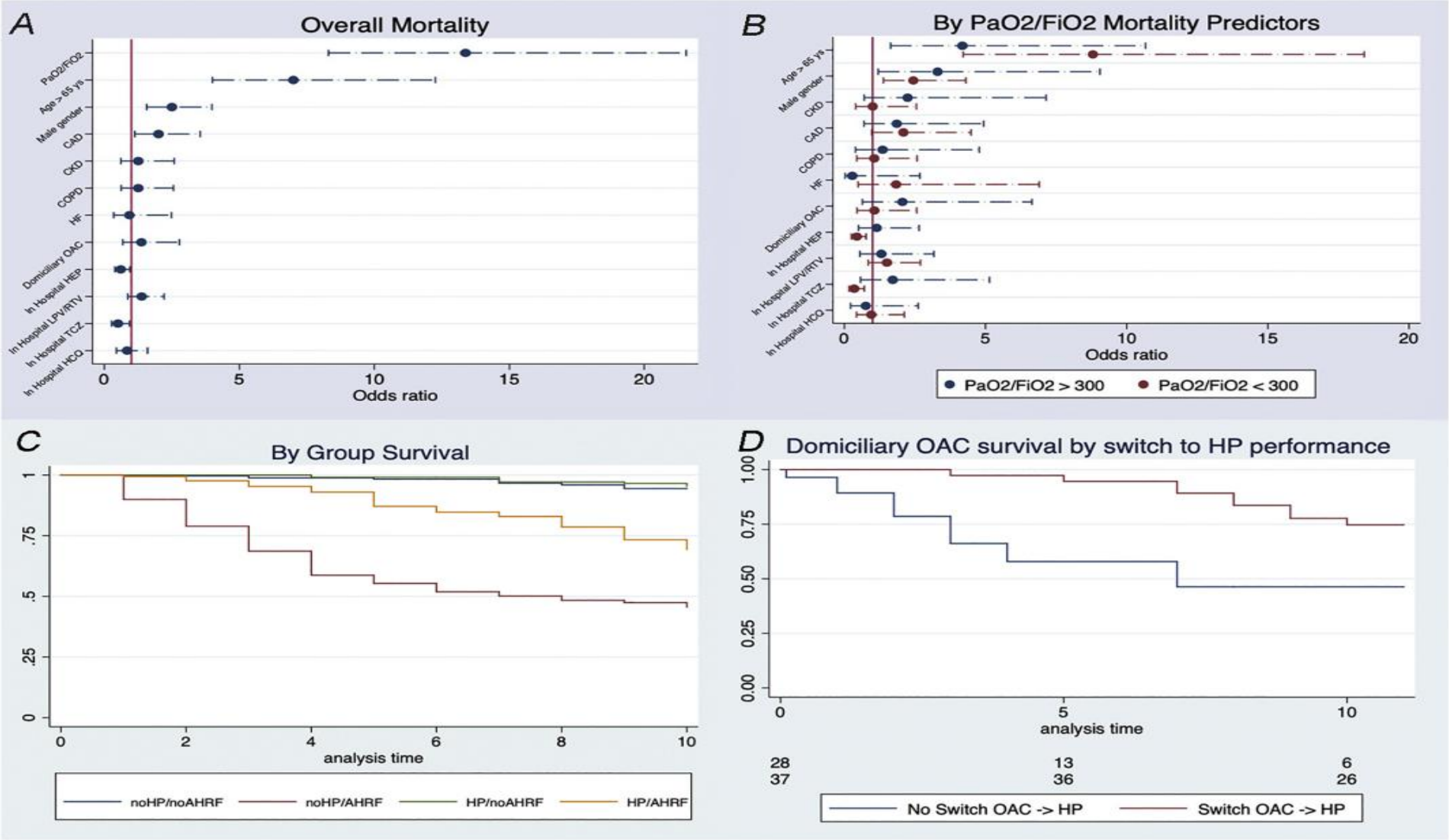
Kết quả từ một phân tích tổng quan

Y. Wang, G. Ao, B. Nasr et al. American Journal of Emergency Medicine 43 (2021) 27–29

VAI TRÒ CỦA KHÁNG ĐÔNG UỐNG TRÊN BỆNH NHÂN SARS-CoV 2



M. Schiavone, A. Gasperetti, M. Mancone et al. International Journal of Cardiology 323 (2021) 276–280

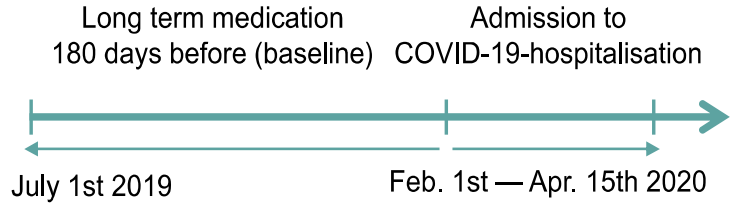
VAI TRÒ CỦA KHÁNG ĐÔNG UỐNG TRÊN BỆNH NHÂN SARS-CoV 2

Impact of long-term oral anticoagulation on clinical outcomes in COVID-19

patient cohort

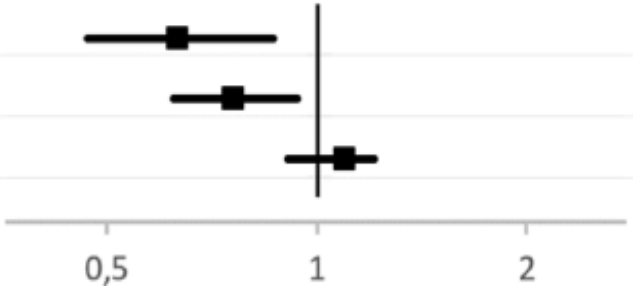
6 637 patients hospitalised with COVID-19 → baseline medication
3.4% VKA
7.7% DOACs
13.7% antiplatelet drugs

timeline



therapy & outcome

Antithrombotic Therapy	Adjusted OR (95% CI)
Vitamin K antagonists	0.57 (0.40-0.83)
DOACs	0.71 (0.56-0.91)
Antiplatelet drugs	1.10 (0.88-1.23)

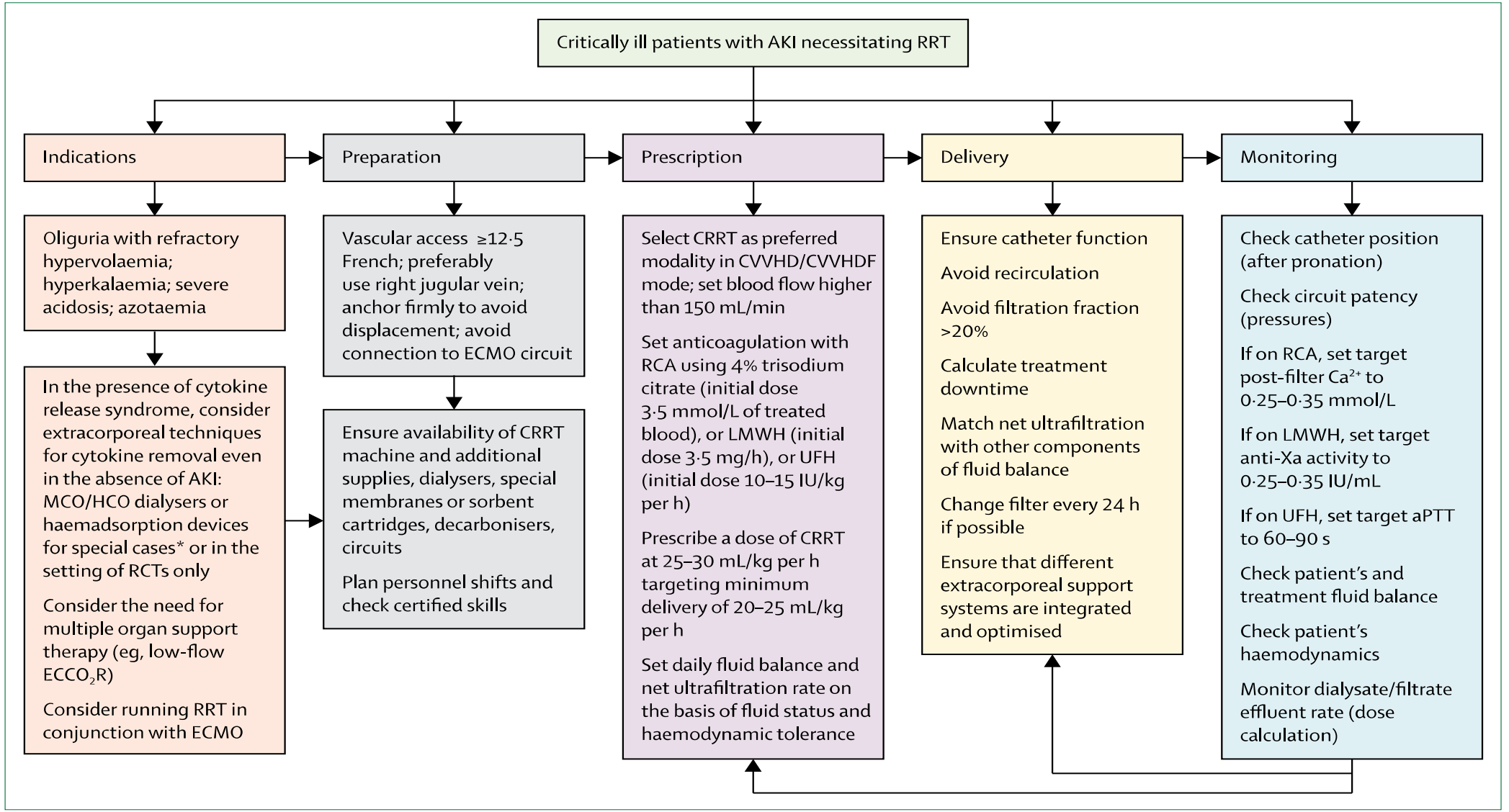


Odds ratio for all-cause mortality or need for ventilation or ECMO

Sử dụng kháng đông uống dài hạn có vai trò bảo vệ?

Georg M. Fröhlich ,Clinical Research in Cardiology, 2021

KHÁNH ĐÔNG TRÊN BỆNH NHÂN SARS-CoV 2 ĐƯỢC ĐIỀU TRỊ THAY THẾ THẬN

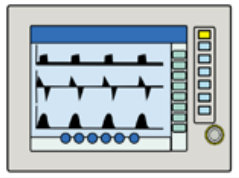


Claudio Ronco ,***Lancet Respir Med*** **2020**

KHÁNG ĐÔNG TRÊN BỆNH NHÂN SARS-CoV 2 ĐƯỢC HỖ TRỢ ECMO THEO CẬP NHẬT CỦA ELSO 2021

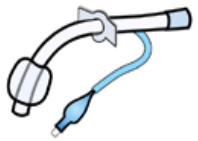
Management strategy or procedure

Pulmonary



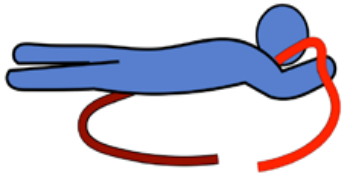
Mechanical Ventilation

No data to suggest deviation from commonly performed low-volume, low-pressure ventilator management for COVID-19 patients receiving ECMO for pulmonary support.



Tracheostomy

Percutaneous tracheostomy appears to be safe and feasible for patients with COVID-19.



Prone positioning

Prone positioning during ECMO is feasible, data are preliminary (demonstrate a potential association with lower mortality) but a recommendation cannot be offered at this time.

Awake ECMO

Early extubation strategy with awake ECMO may be feasible in COVID-19, but insufficient evidence to support recommendation.

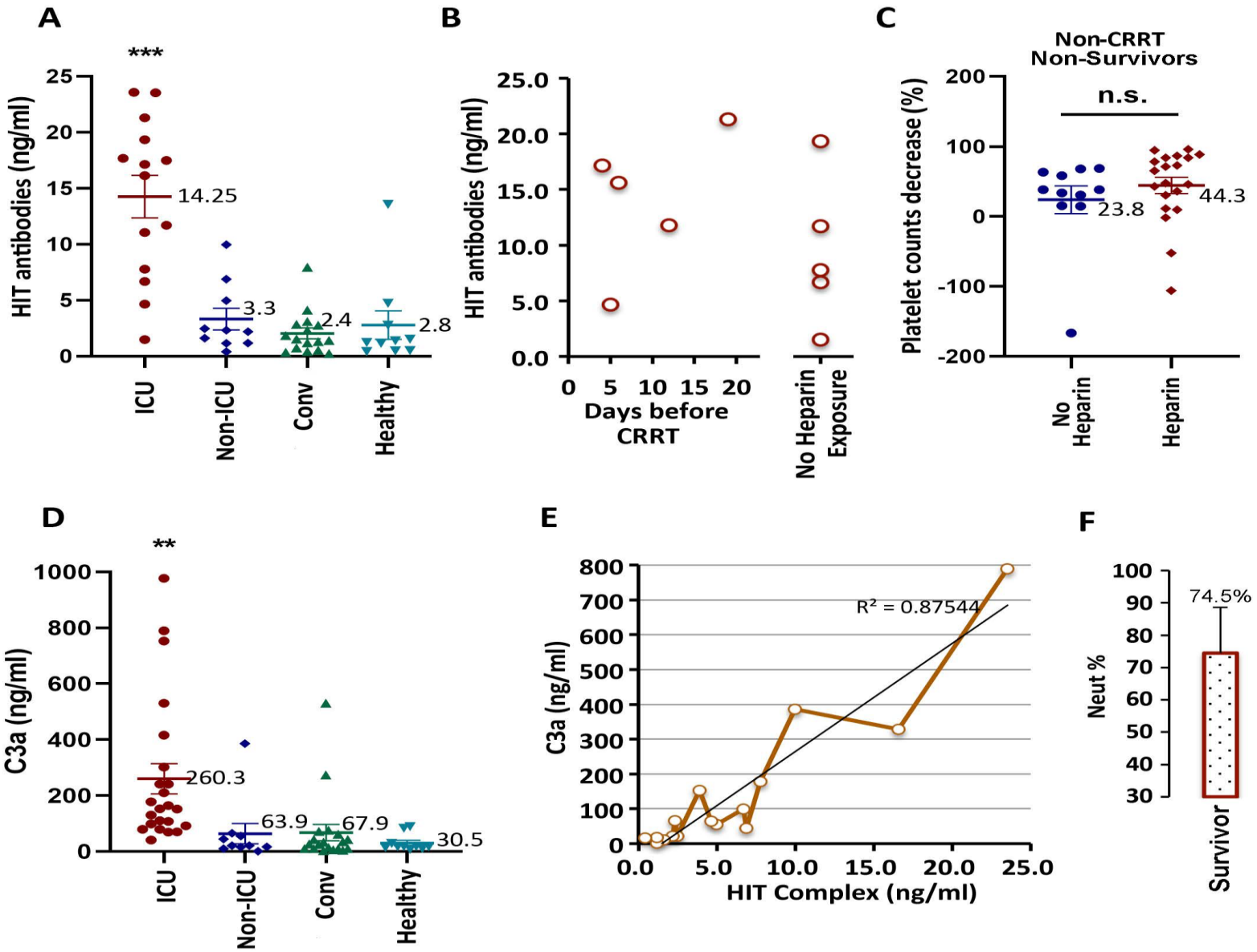
Coagulopathy

COVID-19-induced coagulopathy appears to increase risk of both thrombotic and hemorrhagic events; however, normalized to run duration, rates of bleeding and circuit clotting similar to historical data: insufficient data to suggest deviation from usual anticoagulation practices on ECMO.

- ELSO không khuyến cáo thay đổi phác đồ kháng đông so với guide sử dụng kháng đông 2014
- Lưu ý tầm soát DVT sau rút canula ECMO

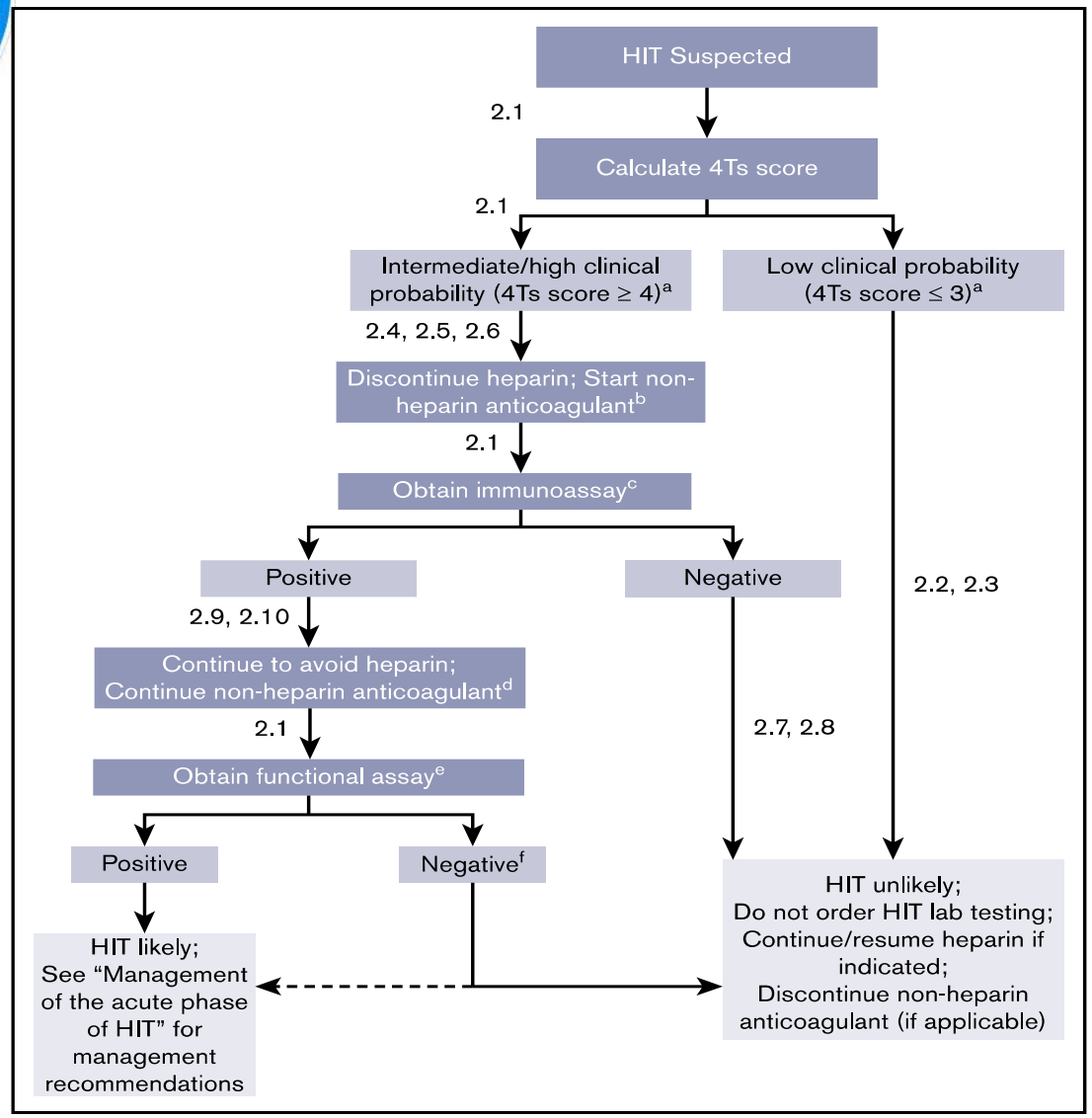
ELSO UPDATE 2021

HIT TRÊN BỆNH NHÂN SARS-CoV2



https://doi.org/10.1101/2020.04.23.2007685

CHẨN ĐOÁN GIẢM TIỂU CẦU DO HEPARIN



Category	2 points	1 point	0 point
Thrombocytopenia	> 50% fall, or nadir ≥ 20 x 10^9/L	30–50% fall, or nadir 10-19 x 10^9/L	< 30% fall, or nadir < 10 x 10^9/L
Timing of the decrease in platelet count	Days 5 to 10, or ≤ day 1 with recent heparin (past 30 days)	> Day 10 or timing unclear, or < day 1 if heparin exposure within past 30-100 days	< Day 4 (no recent heparin)
Thrombosis or other sequelae	Proven thrombosis, skin necrosis, or acute systemic reaction after heparin bolus	Progressive, recurrent, or silent thrombosis; erythematous skin lesions	None
Other causes of thrombocytopenia	None evident	Possible	Definite

0 to 3 points: Low probability (risk of HIT <1 percent)
4 to 5 points: Intermediate probability (risk of HIT ~10%)
6 to 8 points: High probability (risk of HIT~50%)
(4)

ASH 2018 VTE GUIDELINES: HIT

Table 2. Non-heparin anticoagulants for treatment of acute HIT

Drug	Mechanism of action	Route of administration	Primary mechanism of elimination (half-life)	Dosing	Laboratory monitoring
Argatroban	Direct thrombin inhibitor	IV	Hepatobiliary (40-50 min)	Bolus: none Continuous infusion: Normal organ function → 2 μg/kg/min Liver dysfunction (bilirubin >1.5 mg/dL) → 0.5-1.2 μg/kg/min Heart failure, anasarca, postcardiac surgery → 0.5-1.2 μg/kg/min	Adjust to APTT 1.5-3.0 times baseline
Bivalirudin*	Direct thrombin inhibitor	IV	Enzymatic (25 min)	Bolus: none Continuous infusion: Normal organ function → 0.15 mg/kg/h Renal or liver dysfunction → dose reduction may be appropriate	Adjust to APTT 1.5-2.5 times baseline
Danaparoid	Indirect factor Xa inhibitor	IV	Renal (24 h)	Bolus: <60 kg, 1500 units 60-75 kg, 2250 units 75-90 kg, 3000 units >90 kg, 3750 units Accelerated initial infusion: 400 units/h × 4 h, then 300 units/h × 4 h Maintenance infusion: Normal renal function → 200 units/h Renal dysfunction → 150 units/h	Adjust to danaparoid-specific anti-Xa activity of 0.5-0.8 units/mL
Fondaparinux*	Indirect factor Xa inhibitor	SC	Renal (17-24 h)	<50 kg → 5 mg once per day 50-100 kg → 7.5 mg once per day >100 kg → 10 mg once per day	None
Apixaban*†	Direct factor Xa inhibitor	PO	Hepatic (8-15 h)	HITT: 10 mg twice per day × 1 week, then 5 mg twice per day Isolated HIT: 5 mg twice per day until platelet count recovery	None
Dabigatran*†	Direct thrombin inhibitor	PO	Renal (12-17 h)	HITT: 150 mg twice per day after ≥5 days of treatment with a parenteral non-heparin anticoagulant Isolated HIT: 150 mg twice per day until platelet count recovery	None
Rivaroxaban*†	Direct factor Xa inhibitor	PO	Renal (5-9 h)	HITT: 15 mg twice per day × 3 weeks, then 20 mg once per day Isolated HIT: 15 mg twice per day until platelet count recovery	None

XIN CÁM ƠN
CÁC ANH CHỊ ĐỒNG NGHIỆP
ĐÃ CHÚ Ý LẮNG NGHE