International Federation of Clinical Chemistry and Laboratory Medicine

ECAT FOUNDATION

15 and 16 September 2022

CORPUS Congress Centre
Leiden, The Netherlands

International Laboratory Symposium in the field of Thrombosis and Haemostasis

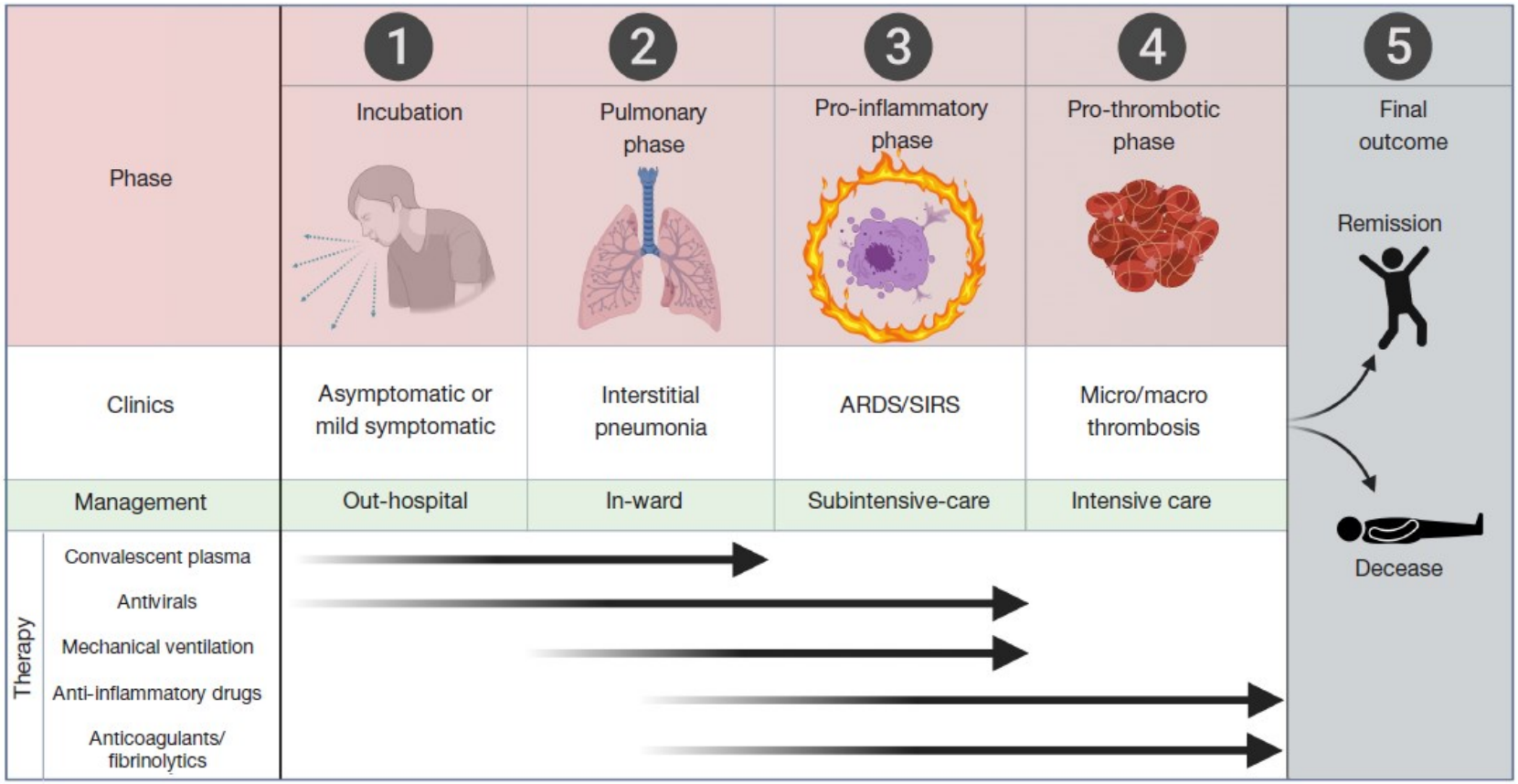
COVID19 and the role of the haemostasis laboratory

Giuseppe Lippi

Ann Transl Med 2020;8(11):693

COVID-19: unravelling the clinical progression of nature's virtually perfect biological weapon

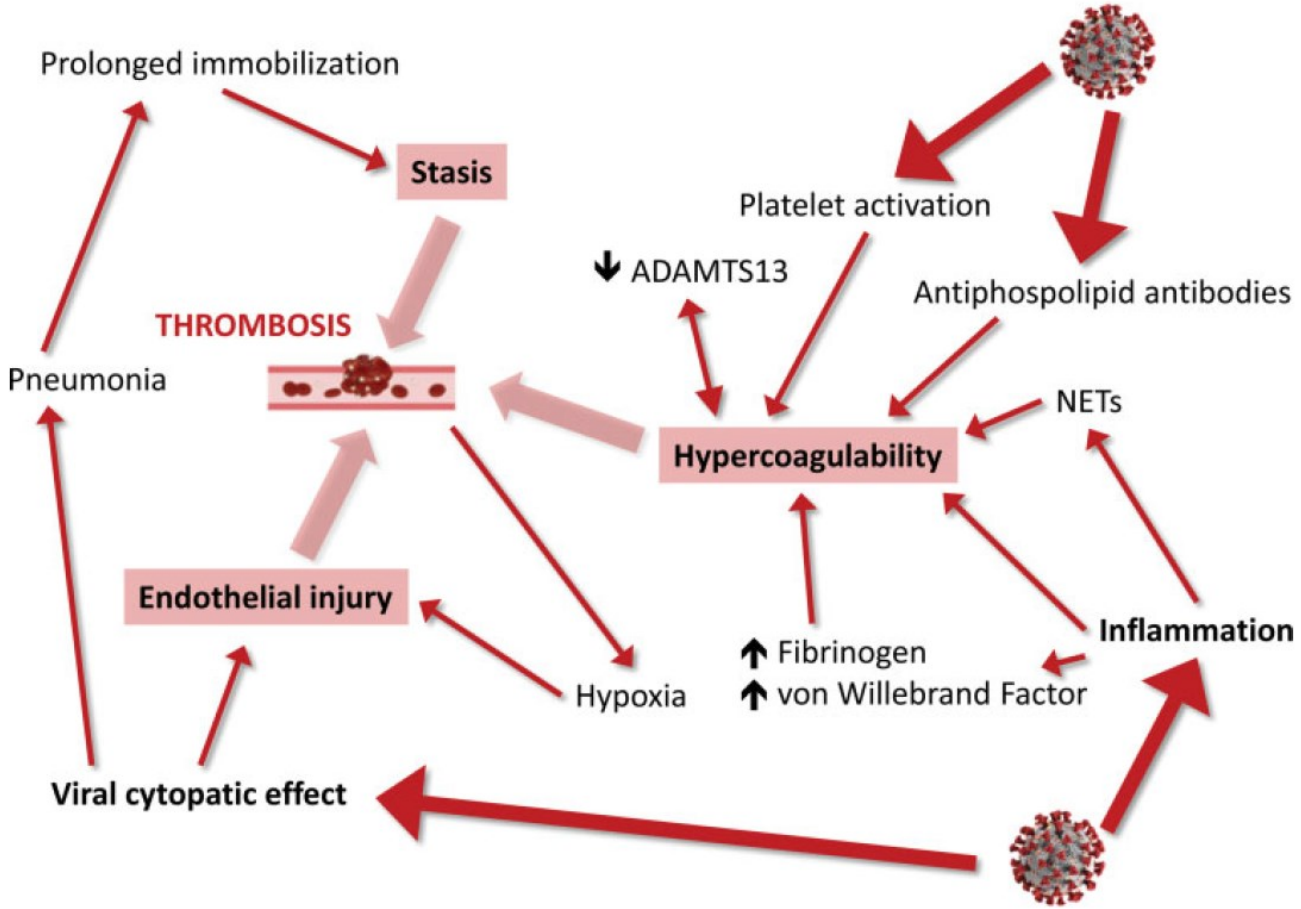
Giuseppe Lippi[1], Fabian Sanchis-Gomar[2,3#], Brandon M. Henry[4#]



Semin Thromb Hemost 2021;47:333–337

Maintaining Hemostasis and Preventing Thrombosis in Coronavirus Disease 2019 (COVID-19): Part II

Emmanuel J. Favaloro, PhD, FFSc (RCPA)[1] Giuseppe Lippi, MD[2]



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Clinical and Applied Thrombosis/Hemostasis 2020 Volume 26: 1-11

COVID-19-Associated Coagulopathy: An Exacerbated Immunothrombosis Response

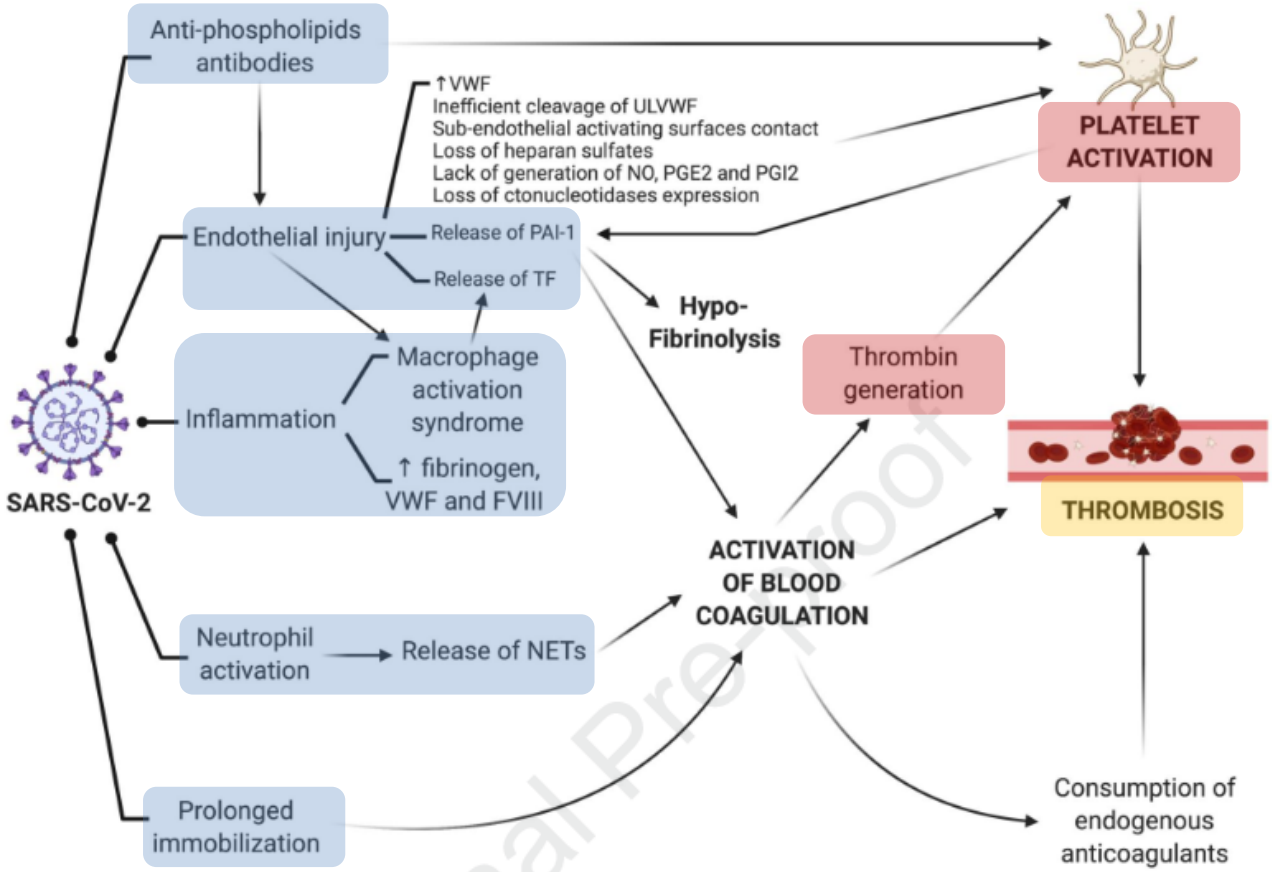
Apoorva Jayarangaiah, MD[1], Pramod Theetha Kariyanna, MD[2], Xiaoyi Chen, MD[3], Amog Jayarangaiah, MD[4], and Abhishek Kumar, MD[1]

Immunothrombosis describes the active participation of the innate immune system in forming a thrombus via distinct cellular and molecular interactions, triggered by recognition of pathogens and damaged cells. Under this theory, this response is proposed to be a conserved evolutionary defensive link to inhibit pathogen dissemination.

Mayo Clin Proc. 2021;96(1):203-217

Coronavirus Disease 2019—Associated Coagulopathy

Giuseppe Lippi, MD; Fabian Sanchis-Gomar, MD, PhD; Emmanuel J. Favaloro, PhD; Carl J. Lavie, MD; and Brandon M. Henry, MD



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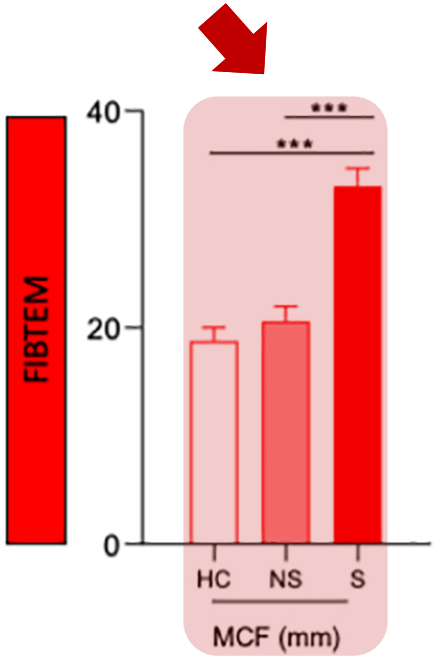
PLoS One. 2022 Jan 14;17(1):e0262600. doi: 10.1371/journal.pone.0262600. eCollection 2022.

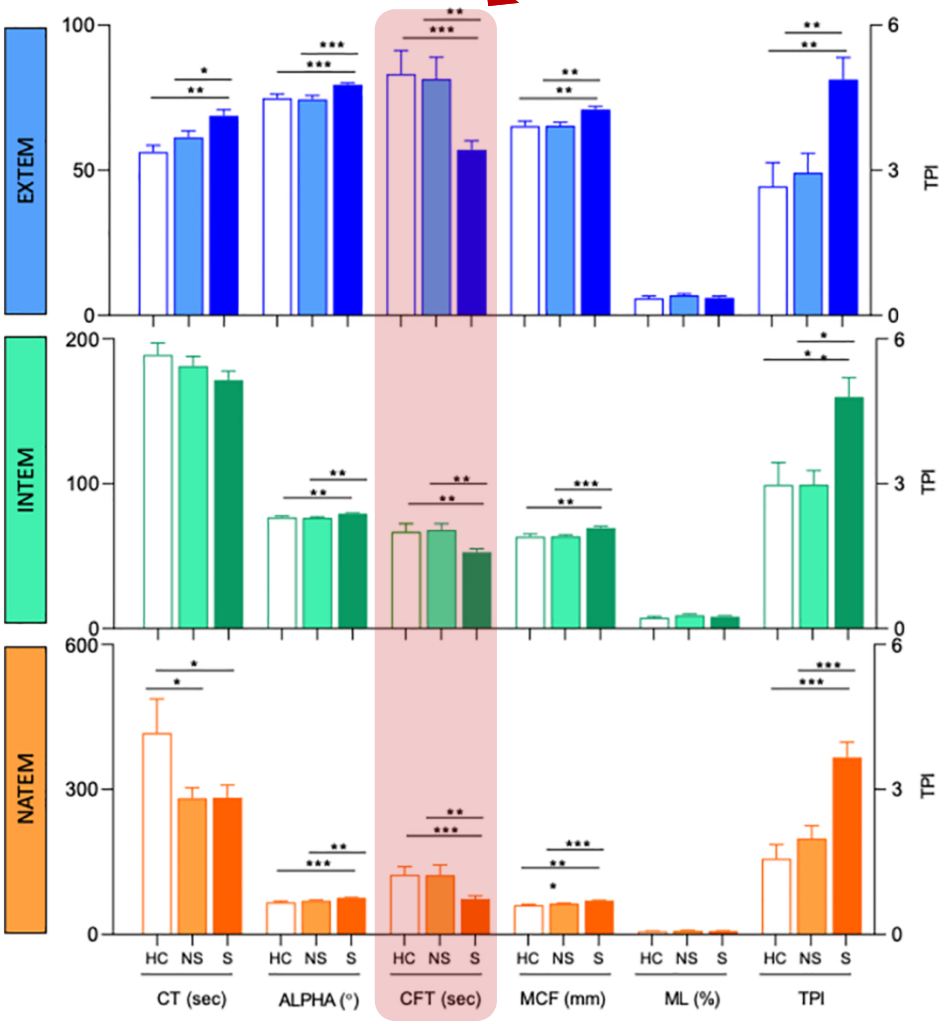
Thromboelastometry demonstrates endogenous coagulation activation in nonsevere and severe COVID-19 patients

Rodrigo B Aires [1 2], Alexandre A de S M Soares [1], Ana Paula M Gomides [3], André M Nicola [1],

Hypercoagulability



Hypercoagulability

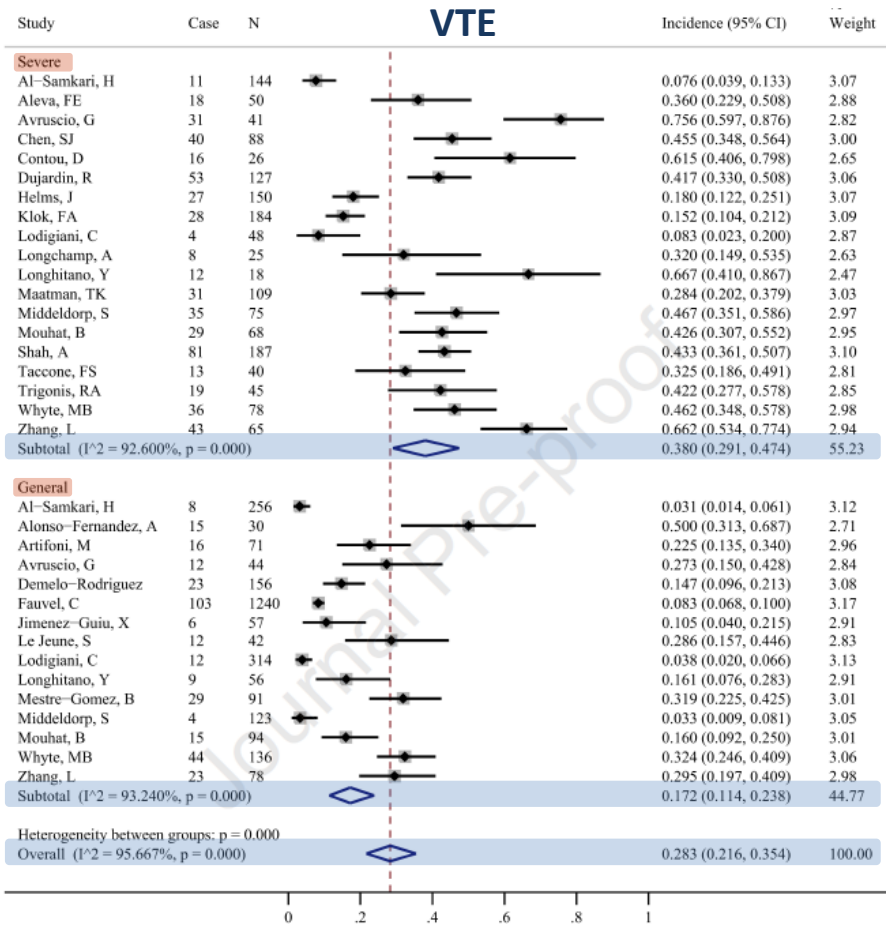


J Vasc Surg Venous Lymphat Disord. 2021 Jan 30;S2213-333X(21)00072-X.

The Incidence, Prognosis and Laboratory Indicators of Venous Thromboembolism in Hospitalized Patients with COVID-19: A Systematic Review and Meta-analysis

Yandong Liu [1], Jiawei Cai [1], Chao Wang [1], Jie Jin [1], Lefeng Qu [2]

VTE

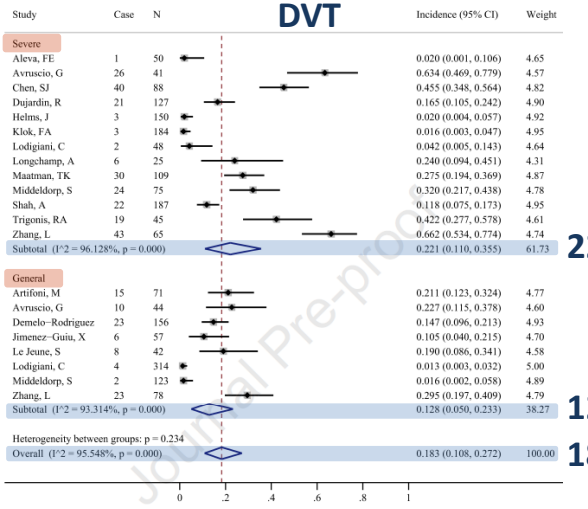


38.0%

17.2%

28.3%

DVT

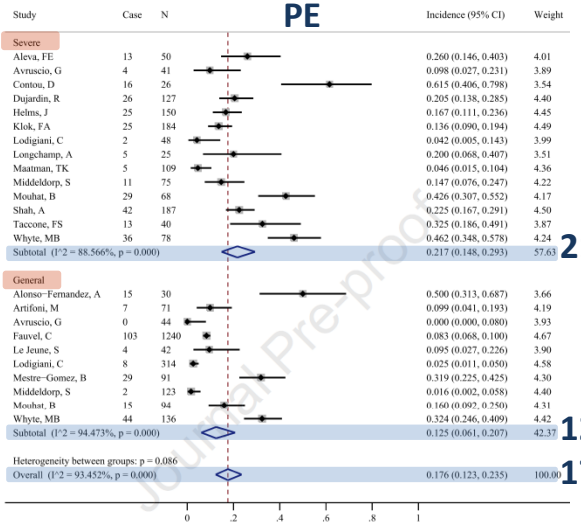


22.1%

12.8%

18.3%

PE



21.7%

12.5%

17.6%

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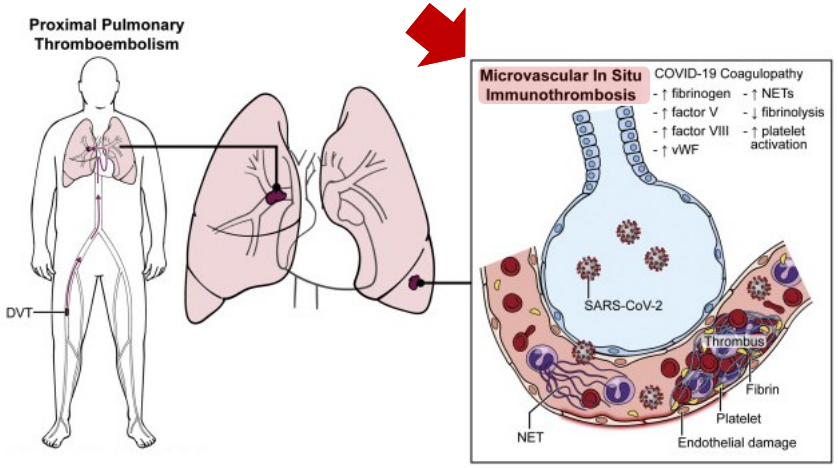
Thromb Res. 2022 Aug 28;218:171-176. doi: 10.1016/j.thromres.2022.08.021. Online ahead of print.

Thromboembolic events in deceased patients with proven SARS-CoV-2 infection: Frequency, characteristics and risk factors

Minna Voigtlaender [1], Carolin Edler [2], Moritz Gerling [2], Julia Schädler [2], Benjamin Ondruschka [2],

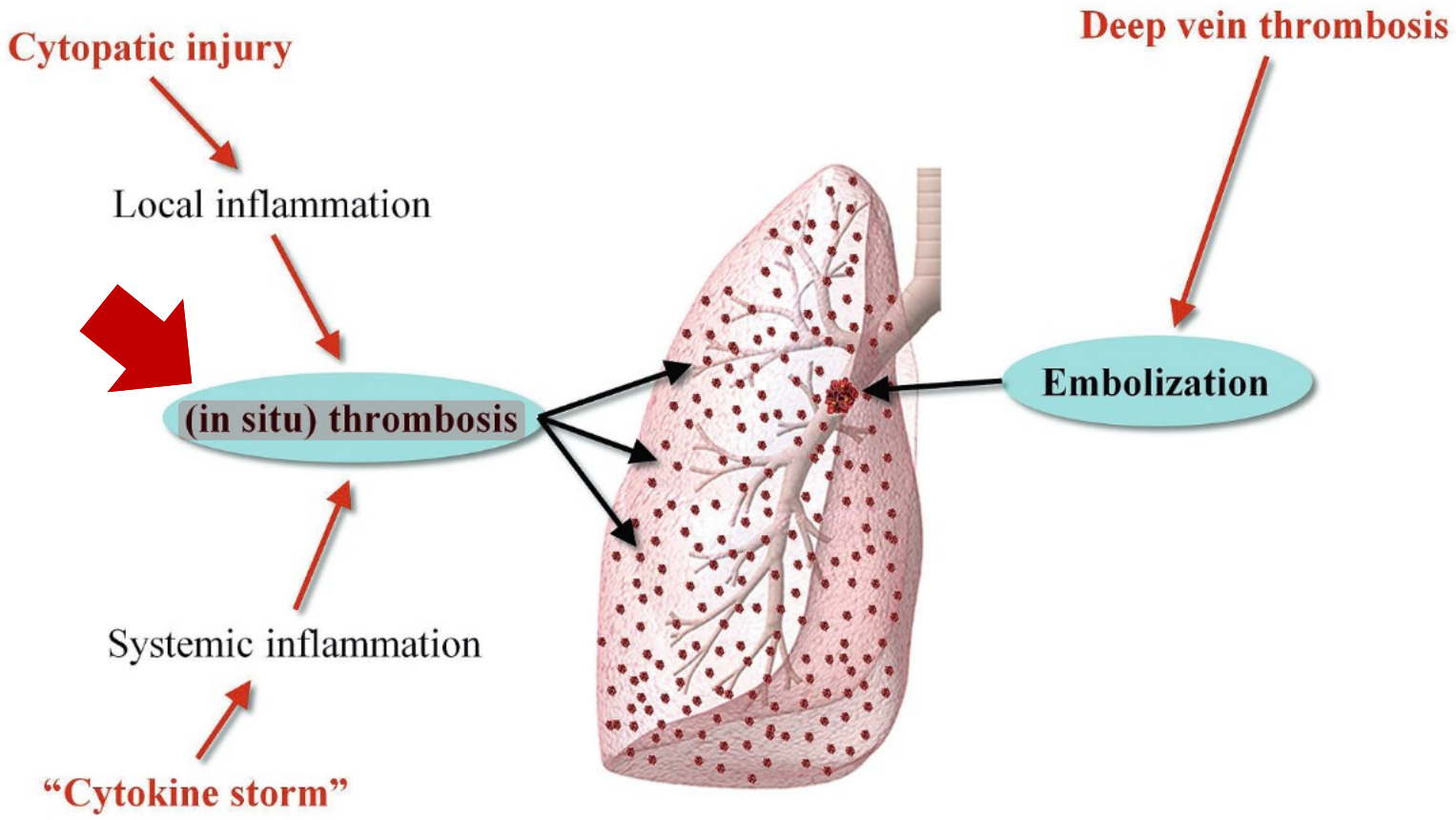


	Number of patients (%)
Any TE	43 (100)
VTE[a]	40 (93.0)
PT	23 (57.5)
PT with lower-extremity DVT	20 (87.0)
PT with proximal DVT (±distal)[b]	4 (20.0)
PT with isolated distal DVT[c]	16 (80.0)
PT without lower-extremity DVT[d]	3 (13.0)
PT in segmental and/or subsegmental arteries only	16 (70.0)

Semin Thromb Hemost. 2022 Jan 12. doi: 10.1055/s-0041-1742091. Online ahead of print.

What We Know (and Do not Know) Regarding the Pathogenesis of Pulmonary Thrombosis in COVID-19

Giuseppe Lippi [1], Emmanuel J Favaloro [2 3 4]



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Circulation. 2022 Mar 22;145(12):940-942. doi: 10.1161/CIRCULATIONAHA.121.057394.

Inherited Thrombophilias Are Associated With a Higher Risk of COVID–19–Associated Venous Thromboembolism: A Prospective Population–Based Cohort Study

Hannah Stevens [# 1 2 3], Rodrigo Canovas [# 4], Huyen Tran [2], Karlheinz Peter [# 5 3], James D McFadyen [# 2 3 6]

Association of Genetic Thrombophilia With Venous Thromboembolism and Mortality in Individuals With COVID-19

Predictor	Odds ratio* (95% CI) for COVID-19 VTE	Odds ratio* (95% CI) for COVID-19 mortality
rs6025	1.80 (1.03–2.92)	1.23 (0.89–1.68)
rs1799963	1.04 (0.36–2.33)	1.06 (0.64–1.68)
rs2519093	0.94 (0.68–1.31)	1.18 (1.00–1.40)
rs8176645	0.83 (0.56–1.21)	1.05 (0.86–1.27)
rs2066865	1.35 (1.07–1.68)	0.99 (0.88–1.12)
rs4253416	1.06 (0.86–1.30)	0.96 (0.87–1.07)
Polygenic risk score-VTE	1.26 (1.08–1.47)	1.01 (0.93–1.10)
Polygenic risk score-ABO	0.97 (0.76–1.23)	1.10 (0.98–1.25)
COVID-19 VTE	–	2.77 (1.91–3.95)

FVL

Fbg-γ

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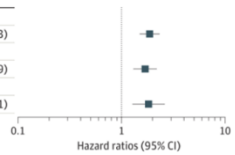
JAMA Intern Med. 2022 Aug 18. doi: 10.1001/jamainternmed.2022.3858. Online ahead of print.

Clinical and Genetic Risk Factors for Acute Incident Venous Thromboembolism in Ambulatory Patients With COVID-19

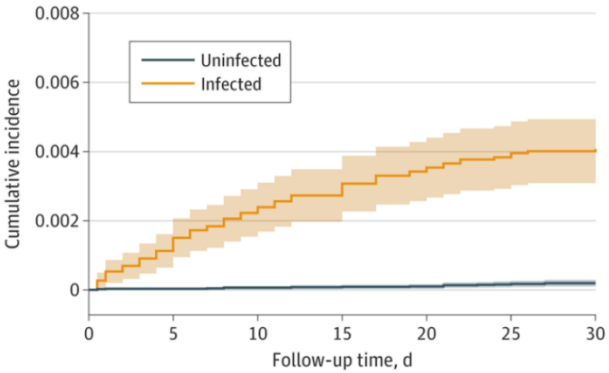
JunQing Xie [1], Albert Prats-Uribe [1], Qi Feng [2], YunHe Wang [2], Dipender Gill [3 4 5], Roger Paredes [6], Dani Prieto-Alhambra [1]

Hazard Ratio of Clinical Risk Factors for Venous Thromboembolism

Variable	Hazard ratios (95% CI)
Age (per 10-y increase)	
Infection-related VTE	1.87 (1.50-2.33)
Sex (male vs female)	
Infection-related VTE	1.69 (1.30-2.19)
Obesity (BMI ≥30 vs <30)	
Infection-related VTE	1.83 (1.28-2.61)



SARS-CoV-2 infection: HR, 21.4 (95%CI, 12.6-36.3)



Inherited Thrombophilia With Venous Thromboembolism Among Patients COVID-19[a]

	Primary outcome, venous thromboembolism		
	HR (95% CI)		
Exposure	Unadjusted	Adjusted	*P* value
Inherited thrombophilia[b]	1.82 (1.02-3.23)	2.05 (1.15-3.66)	.01
Factor V Leiden	1.97 (1.03-3.76)	2.17 (1.13-4.15)	.02
Prothrombin G20210A[c]	1.31 (0.42-4.11)	1.52 (0.48-4.79)	.45

Thromb Res. 2021 Dec 7;209:94-98. doi: 10.1016/j.thromres.2021.11.029. Online ahead of print.

Incidence of venous thromboembolic events in COVID-19 patients after hospital discharge: A systematic review and meta-analysis

Marco Zuin [1], Matthias M Engelen [2], Stefano Barco [3], Alex C Spyropoulos [4], Thomas Vanassche [2],

Follow-up: 62 days (21-180 days)

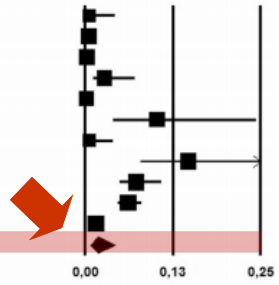
- ✓Venous thromboembolism: **1.8%** (0.8-4.1%)
- ✓Pulmonary embolism: **1.5%** (0.5-4.0%)
- ✓Deep vein thrombosis: **0.8%** (0.3-2.1%)

A - Venous Thromboembolism

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Patell	0,006	0,001	0,042	-5,072	0,000	6,71
Roberts	0,005	0,002	0,009	-15,968	0,000	9,72
Lund	0,002	0,001	0,004	-27,172	0,000	10,03
Engelen	0,027	0,010	0,071	-7,041	0,000	9,06
Rashidi	0,002	0,001	0,006	-10,783	0,000	8,75
Vlachou	0,103	0,039	0,243	-4,110	0,000	8,97
Bourguignon	0,006	0,001	0,039	-5,144	0,000	6,71
Parra	0,148	0,079	0,260	-4,858	0,000	9,63
Salisbury	0,073	0,048	0,108	-11,506	0,000	10,03
Venturelli	0,061	0,046	0,081	-18,127	0,000	10,17
Giannis	0,015	0,012	0,019	-35,914	0,000	10,22
Random effect:	0,018	0,008	0,041	-9,088	0,000	

Statistics for each study | Weight (Random) | Event rate and 95% CI

Tau-squared: 1.88; Q value: 280.0
I-squared: 96.0%, p<0.0001

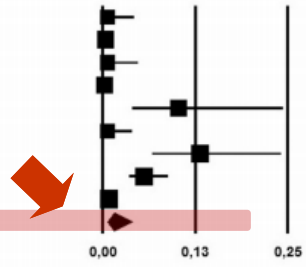


B - Pulmonary Embolism

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Patell	0,006	0,001	0,042	-5,072	0,000	8,88
Roberts	0,004	0,002	0,008	-14,756	0,000	12,31
Engelen	0,007	0,001	0,047	-4,960	0,000	8,87
Rashidi	0,002	0,001	0,006	-10,783	0,000	11,34
Vlachou	0,103	0,039	0,243	-4,110	0,000	11,61
Bourguignon	0,006	0,001	0,039	-5,144	0,000	8,88
Parra	0,131	0,067	0,241	-4,985	0,000	12,31
Salisbury	0,056	0,035	0,088	-11,307	0,000	12,78
Giannis	0,009	0,006	0,012	-30,664	0,000	13,01
Random effect:	0,015	0,005	0,040	-8,040	0,000	

Statistics for each study | Weight (Random) | Event rate and 95% CI

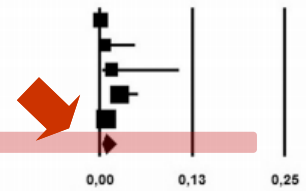
Tau-squared:2.08; Q-value: 122.8
I-squared: 93.4%, p<0.0001



C - Deep vein Thrombosis

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Relative weight
Roberts	0,001	0,000	0,004	-9,673	0,000	18,26
Engelen	0,007	0,001	0,047	-4,960	0,000	12,95
Parra	0,016	0,002	0,107	-4,061	0,000	12,88
Salisbury	0,026	0,013	0,052	-10,068	0,000	26,13
Giannis	0,009	0,007	0,012	-31,069	0,000	29,77
Random effect:	0,008	0,003	0,021	-10,032	0,000	

Tau-squared: 0.73; Q-value: 18.5
I-squared:78.4%, p<0.0001



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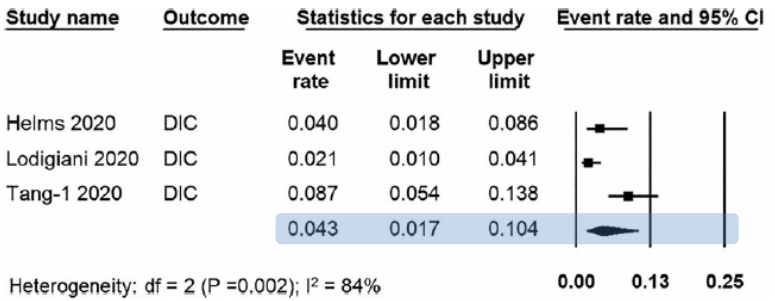
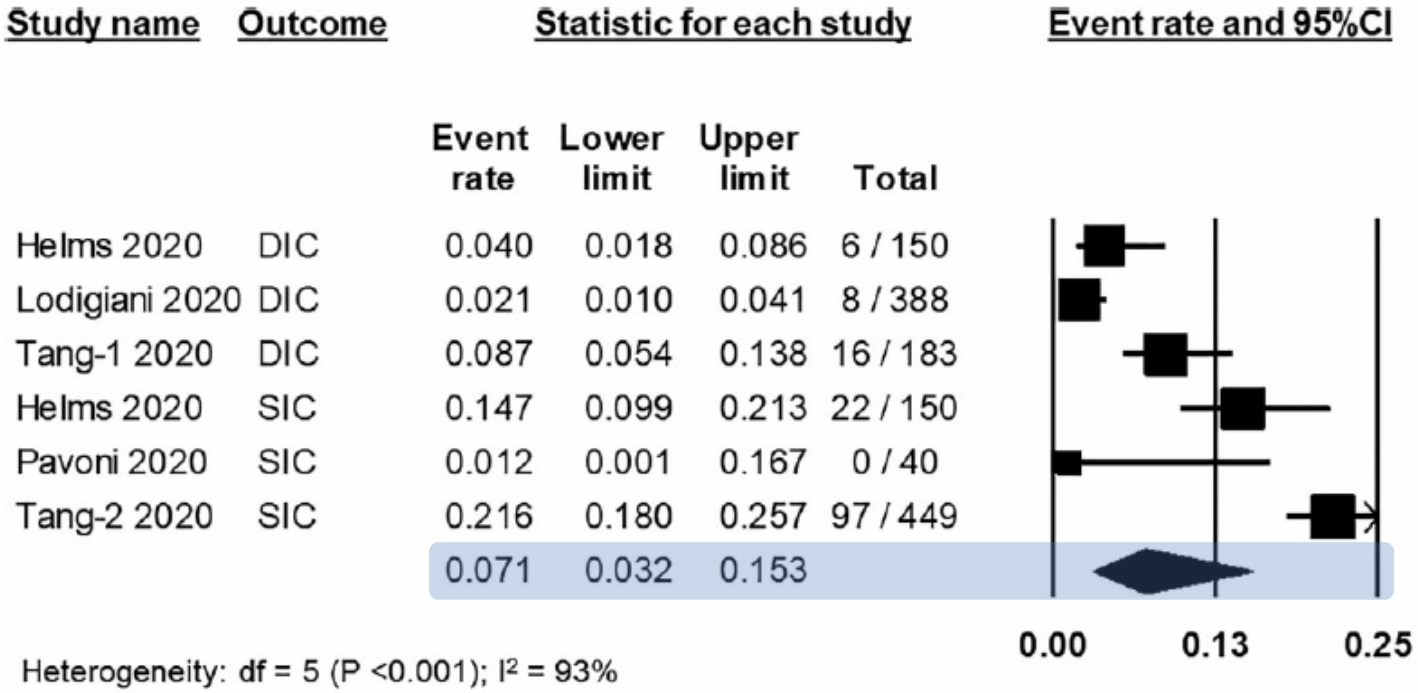
Clinical and Applied Thrombosis/Hemostasis 2021 Volume 27: 1-9

Systemic Coagulopathy in Hospitalized Patients With Coronavirus Disease 2019: A Systematic Review and Meta-Analysis

Noppacharn Uaprasert, MD[1,2], Chatphatai Moonla, MD[2,3], Darintr Sosothikul, MD[4], Ponlapat Rojnuckarin, MD, PhD[1,2], and Thita Chiasakul, MD[1,2]

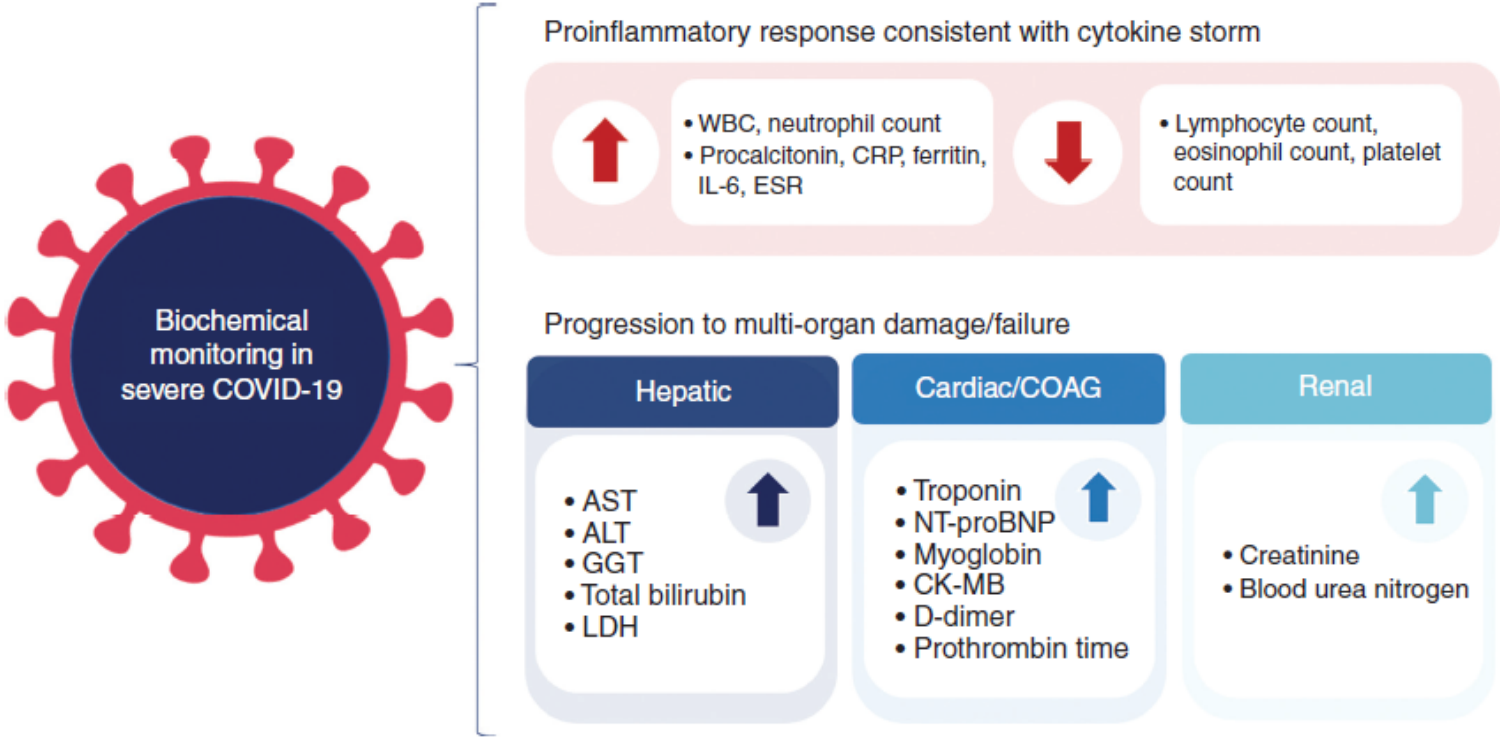




Clin Chem Lab Med. 2020 Jun 25;58(7):1037-1052. doi: 10.1515/cclm-2020-0722.

Molecular, serological, and biochemical diagnosis and monitoring of COVID-19: IFCC taskforce evaluation of the latest evidence

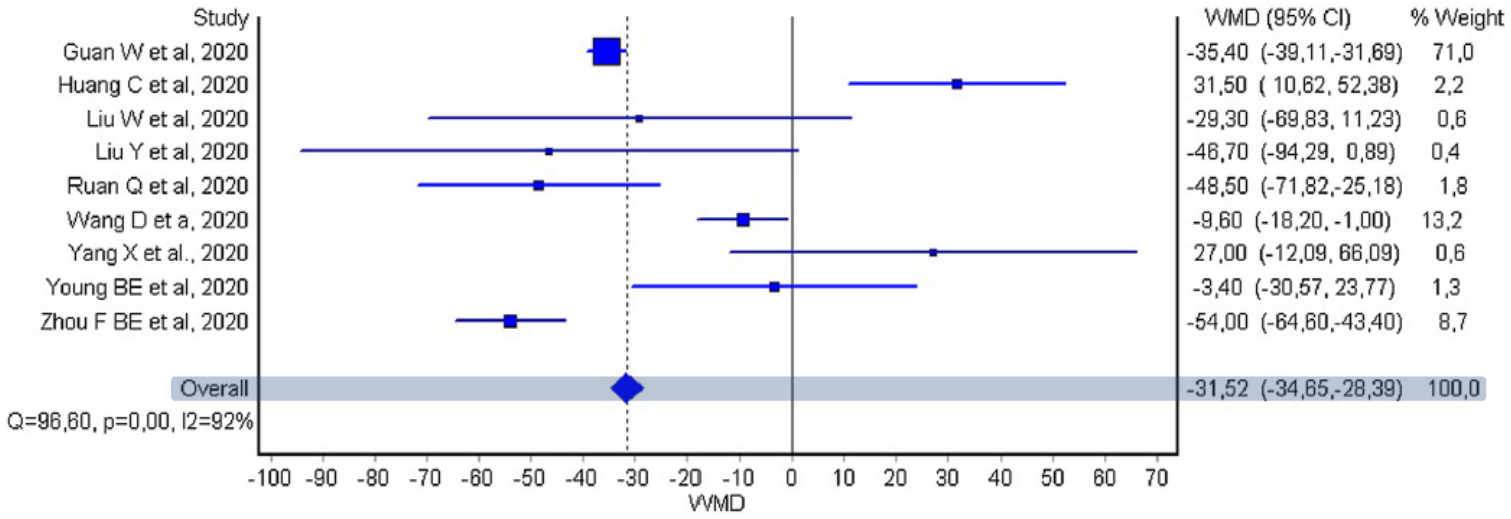
Mary Kathryn Bohn [1], Giuseppe Lippi [2 3], Andrea Horvath [2 4], Sunil Sethi [2 5], David Koch [2 6], Maurizio Ferrari [2 7], Cheng-Bin Wang [2 8], Nicasio Mancini [2 9], Shannon Steele [1], Khosrow Adeli [2 10]



Clinica Chimica Acta 506 (2020) 145–148

Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A *meta*-analysis

Giuseppe Lippi[a], Mario Plebani[b,1], Brandon Michael Henry[c,*,1]



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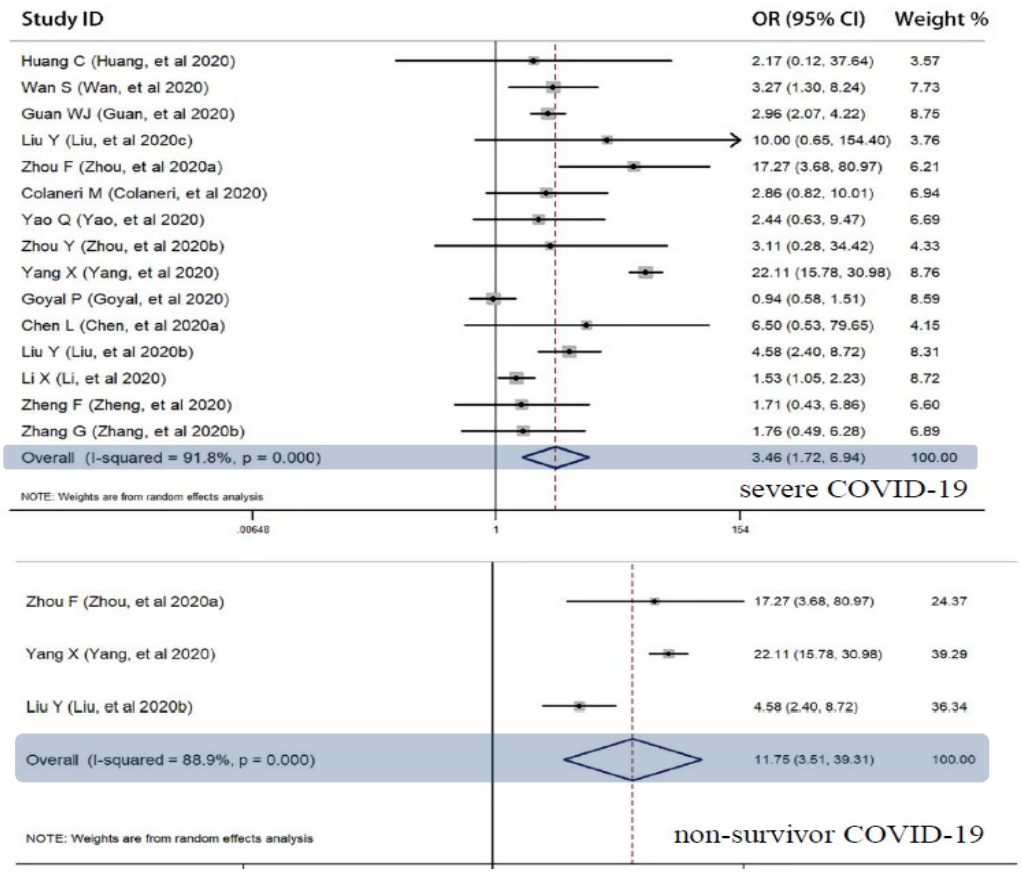
Br J Haematol. 2020 May 18. doi: 10.1111/bjh.16817. Online ahead of print.

The Association Between Severe COVID-19 and Low Platelet Count: Evidence From 31 Observational Studies Involving 7613 Participants

Shi-Qin Jiang [1], Qiu-Fen Huang [2], Wei-Ming Xie [3], Chao Lv [2], Xiao-Qing Quan [4]

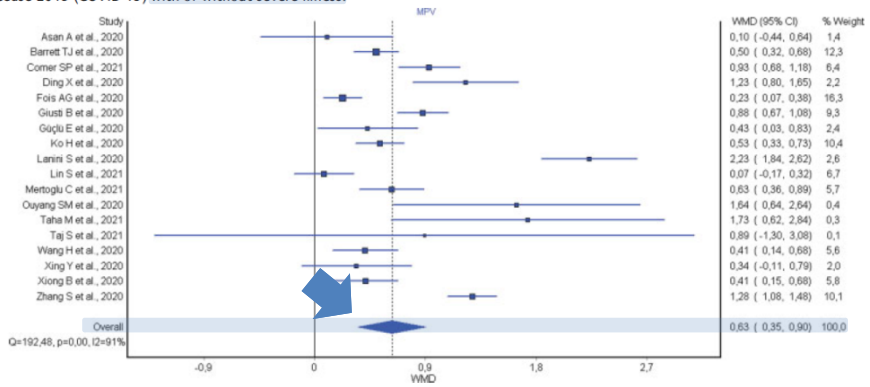


Semin Thromb Hemost 2021;47:456–459.

Mean Platelet Volume Predicts Severe COVID-19 Illness

Giuseppe Lippi, MD[1] Brandon M. Henry, MD[2,*] Emmanuel J. Favaloro, PhD, FFSc, RCPA[3,*]

Fig. 1 Weighted mean difference (WMD) and 95% confidence interval (95% CI) of mean platelet volume (MPV) in patients with coronavirus disease 2019 (COVID-19) with or without severe illness.

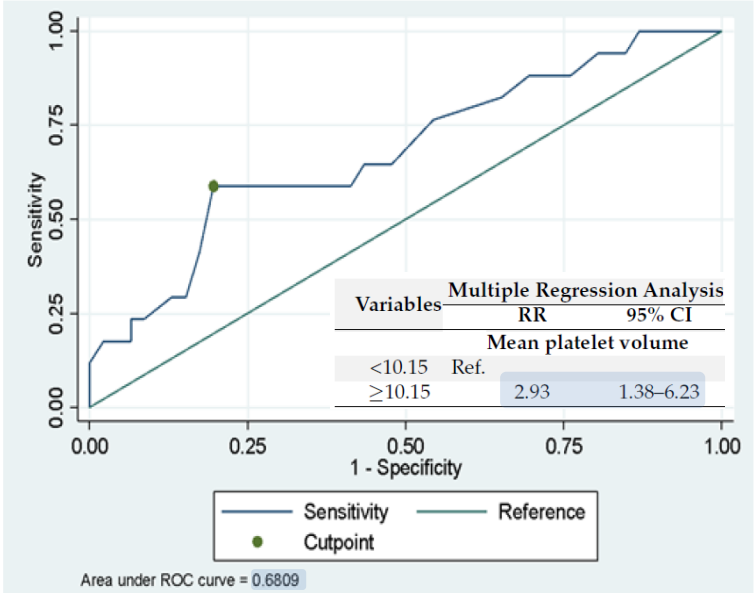


Diseases. 2022 Apr 15;10(2):22. doi: 10.3390/diseases10020022.

Mean Platelet Volume as a Predictor of COVID-19 Severity: A Prospective Cohort Study in the Highlands of Peru

Jhosef Franck Quispe-Pari [1,2], Jose Armando Gonzales-Zamora [3,4], Judith Munive-Dionisio [1],

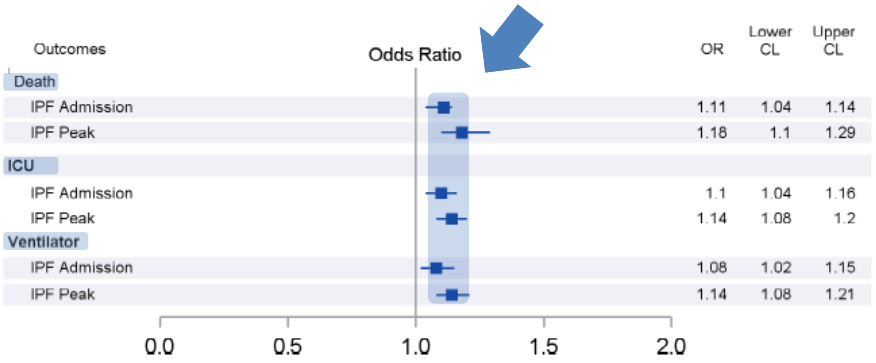
Figure 1. ROC analysis between MPV value and severity of SARS-CoV-2 infection [ROC: 0.6809, 95% CI (0.52664-0.83526)].



Br J Haematol. 2021 Jun 16. doi: 10.1111/bjh.17656. Online ahead of print.

Immature platelets as a biomarker for disease severity and mortality in COVID-19 patients

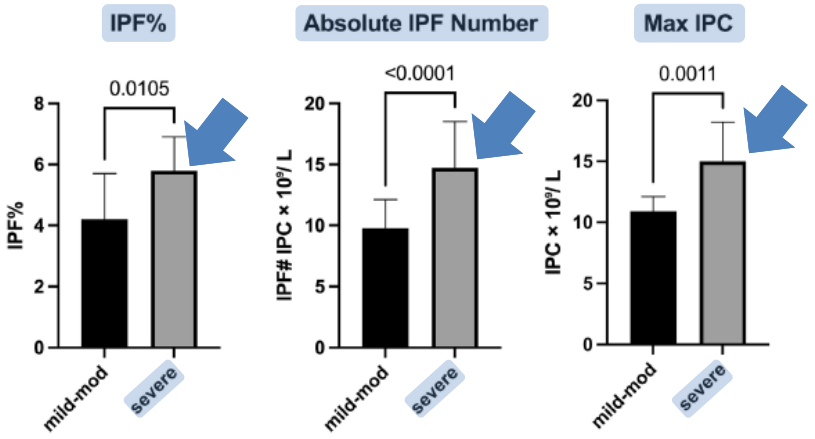
Daniel Welder [1], Haekyung Jeon-Slaughter [2], Bilal Ashraf [3], Sung-Hee Choi [4], Weina Chen [1], Ibrahim Ibrahim [3], Taha Bat [3]



J Thromb Thrombolysis. 2021 Sep 14. doi: 10.1007/s11239-021-02560-x. Online ahead of print.

Immature platelets in patients with Covid-19: association with disease severity

Amir Cohen[1,2] · Emanuel Harari[1,2] · Ella Yahud[1,2] · Michal Cipok[2,3] · Gabriel Bryk[2,3] · Nili Karp Lador[2,4] · Tal Mann[2,4] Ami Mayo[2,4] · Eli I. Lev[1,2,5]



J Pediatr. 2022 Aug 6;S0022-3476(22)00703-X. doi: 10.1016/j.jpeds.2022.07.035. ACTIONS

Immature platelet fraction as a biomarker for disease severity in pediatric respiratory Coronavirus Disease 2019

Nicholas Cj Lee [1], Yusuf Kemal Demir [2], Bilal Ashraf [1], Ibrahim Ibrahim [3], Taha Bat [3], Kathryn E Dickerson [4]

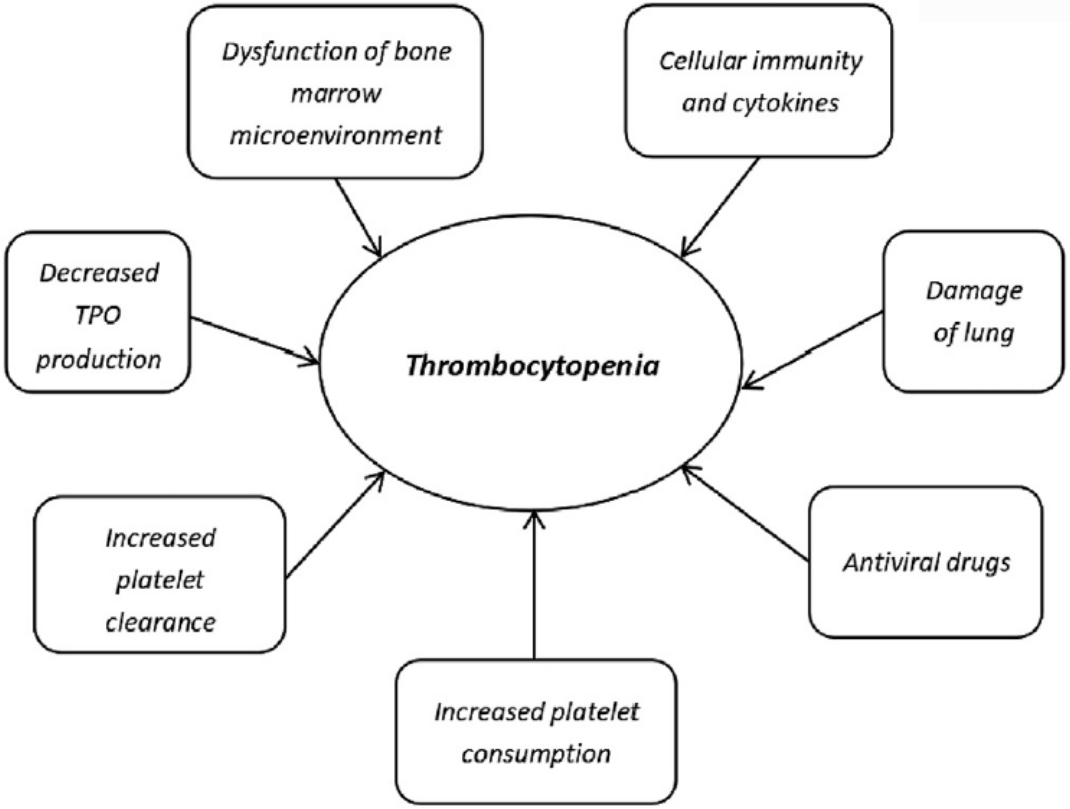
IPF% significantly higher in:

- ✓ Patients admitted to the ICU (7.3 vs non-ICU: 4, P=0.006)
- ✓ Patients placed on ventilation (7.1 vs non-ventilator: 4.2, P=0.01).

Thrombosis Research 193 (2020) 110–115

Mechanisms involved in the development of thrombocytopenia in patients with COVID-19

Yujiao Zhang[a], Xiaoyuan Zeng[a], Yingying Jiao[a], Zongpeng Li[a], Qifa Liu[a], Mo Yang[b,*], Jieyu Ye[a,*]



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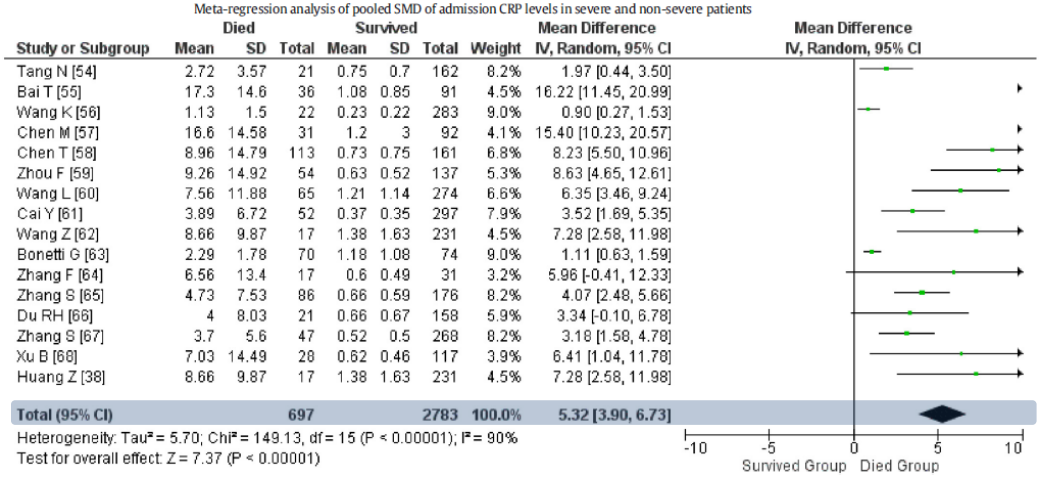
American Journal of Emergency Medicine xxx (2020) xxx

Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis

Baris Gungor, M.D. [a], Adem Atici, M.D. [b], Omer Faruk Baycan, M.D. [b], Gokhan Alici, M.D. [c], Fatih Ozturk, M.D. [d], Sevil Tugrul, M.D. [e], Ramazan Asoglu, M.D. [f], Erdem Cevik, M.D. [g], Irfan Sahin, M.D. [e], Hasan Ali Barman, M.D. [h,*]

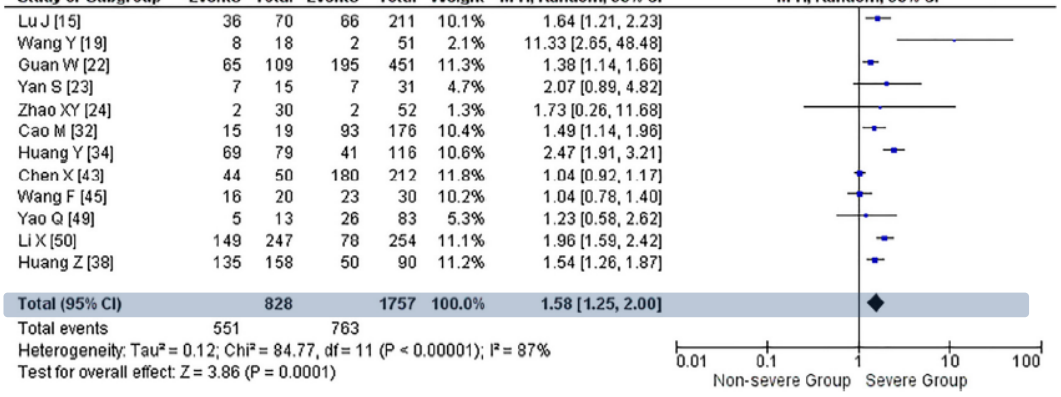
Meta-regression analysis of pooled SMD of admission CRP levels in severe and non-severe patients



Study or Subgroup	Died Mean	SD	Total	Survived Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Tang N [54]	2.72	3.57	21	0.75	0.7	162	8.2%	1.97 [0.44, 3.50]
Bai T [55]	17.3	14.6	36	1.08	0.85	91	4.5%	16.22 [11.45, 20.99]
Wang K [56]	1.13	1.5	22	0.23	0.22	283	9.0%	0.90 [0.27, 1.53]
Chen M [57]	16.6	14.58	31	1.2	3	92	4.1%	15.40 [10.23, 20.57]
Chen T [58]	8.96	14.79	113	0.73	0.75	161	6.8%	8.23 [5.50, 10.96]
Zhou F [59]	9.26	14.92	54	0.63	0.52	137	5.3%	8.63 [4.65, 12.61]
Wang L [60]	7.56	11.88	65	1.21	1.14	274	6.6%	6.35 [3.46, 9.24]
Cai Y [61]	3.89	6.72	52	0.37	0.35	297	7.9%	3.52 [1.69, 5.35]
Wang Z [62]	8.66	9.87	17	1.38	1.63	231	4.5%	7.28 [2.58, 11.98]
Bonetti G [63]	2.29	1.78	70	1.18	1.08	74	9.0%	1.11 [0.63, 1.59]
Zhang F [64]	6.56	13.4	17	0.6	0.49	31	3.2%	5.96 [-0.41, 12.33]
Zhang S [65]	4.73	7.53	86	0.66	0.59	176	8.2%	4.07 [2.48, 5.66]
Du RH [66]	4	8.03	21	0.66	0.67	158	5.9%	3.34 [-0.10, 6.78]
Zhang S [67]	3.7	5.6	47	0.52	0.5	268	8.2%	3.18 [1.58, 4.78]
Xu B [68]	7.03	14.49	28	0.62	0.46	117	3.9%	6.41 [1.04, 11.78]
Huang Z [38]	8.66	9.87	17	1.38	1.63	231	4.5%	7.28 [2.58, 11.98]
Total (95% CI)			**697**			**2783**	**100.0%**	**5.32 [3.90, 6.73]**

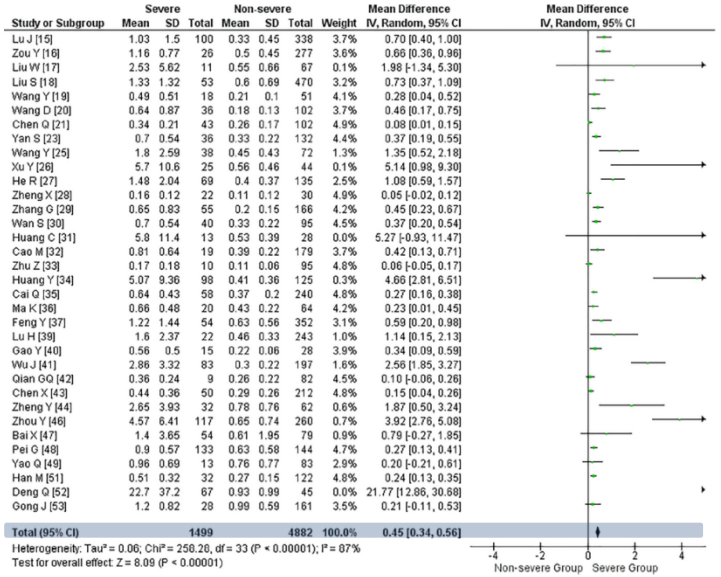
Heterogeneity: Tau² = 5.70; Chi² = 149.13, df = 15 (P < 0.00001); I² = 90%
Test for overall effect: Z = 7.37 (P < 0.00001)

Pooled ORs of the multivariate regression analysis of mortality



Study or Subgroup	Severe Events	Total	Non-severe Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Lu J [15]	36	70	66	211	10.1%	1.64 [1.21, 2.23]
Wang Y [19]	8	18	2	51	2.1%	11.33 [2.65, 48.48]
Guan W [22]	65	109	195	451	11.3%	1.38 [1.14, 1.66]
Yan S [23]	7	15	7	31	4.7%	2.07 [0.89, 4.82]
Zhao XY [24]	2	30	2	52	1.3%	1.73 [0.26, 11.68]
Cao M [32]	15	19	93	176	10.4%	1.49 [1.14, 1.96]
Huang Y [34]	69	79	41	116	10.6%	2.47 [1.91, 3.21]
Chen X [43]	44	50	180	212	11.8%	1.04 [0.92, 1.17]
Wang F [45]	16	20	23	30	10.2%	1.04 [0.78, 1.40]
Yao Q [49]	5	13	26	83	5.3%	1.23 [0.58, 2.62]
Li X [50]	149	247	78	254	11.1%	1.96 [1.59, 2.42]
Huang Z [38]	135	158	50	90	11.2%	1.54 [1.26, 1.87]
Total (95% CI)		**828**		**1757**	**100.0%**	**1.58 [1.25, 2.00]**
Total events	551		763			

Heterogeneity: Tau² = 0.12; Chi² = 84.77, df = 11 (P < 0.00001); I² = 87%
Test for overall effect: Z = 3.86 (P = 0.0001)



Study or Subgroup	Severe Mean	SD	Total	Non-severe Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lu J [15]	1.03	1.5	100	0.33	0.45	338	3.7%	0.70 [0.40, 1.00]
Zou Y [16]	1.16	0.77	26	0.5	0.45	277	3.6%	0.66 [0.36, 0.96]
Liu W [17]	2.53	5.62	11	0.55	0.66	67	0.1%	1.98 [-1.34, 5.30]
Liu S [18]	1.33	1.32	53	0.6	0.69	470	3.2%	0.73 [0.37, 1.09]
Wang Y [19]	0.49	0.51	18	0.21	0.1	51	4.1%	0.28 [0.04, 0.52]
Wang D [20]	0.64	0.87	36	0.18	0.13	102	3.7%	0.46 [0.17, 0.75]
Chen Q [21]	0.34	0.21	43	0.26	0.17	102	4.9%	0.08 [0.01, 0.15]
Yan S [23]	0.7	0.54	36	0.33	0.22	132	4.4%	0.37 [0.19, 0.55]
Wang Y [25]	1.8	2.59	38	0.45	0.43	72	1.3%	1.35 [0.52, 2.18]
Xu Y [26]	5.7	10.6	25	0.56	0.46	44	0.1%	5.14 [0.98, 9.30]
He R [27]	1.48	2.04	69	0.4	0.37	135	2.5%	1.08 [0.59, 1.57]
Zheng X [28]	0.16	0.12	22	0.11	0.12	30	4.9%	0.05 [-0.02, 0.12]
Zhang G [29]	0.65	0.83	55	0.2	0.15	166	4.2%	0.45 [0.23, 0.67]
Wan S [30]	0.7	0.54	40	0.33	0.22	95	4.5%	0.37 [0.20, 0.54]
Huang C [31]	5.8	11.4	13	0.53	0.39	28	0.0%	5.27 [-0.93, 11.47]
Cao M [32]	0.81	0.64	19	0.39	0.22	179	3.7%	0.42 [0.13, 0.71]
Zhu Z [33]	0.17	0.18	10	0.11	0.06	95	4.8%	0.06 [-0.05, 0.17]
Huang Y [34]	5.07	9.36	98	0.41	0.36	125	0.3%	4.66 [2.81, 6.51]
Cai Q [35]	0.64	0.43	58	0.37	0.2	240	4.8%	0.27 [0.16, 0.38]
Ma K [36]	0.66	0.48	20	0.43	0.22	64	4.2%	0.23 [0.01, 0.45]
Feng Y [37]	1.22	1.44	54	0.63	0.56	352	3.1%	0.59 [0.20, 0.98]
Lu H [39]	1.6	2.37	22	0.46	0.33	243	1.0%	1.14 [0.15, 2.13]
Gao Y [40]	0.56	0.5	15	0.22	0.06	28	3.9%	0.34 [0.09, 0.59]
Wu J [41]	2.86	3.32	83	0.3	0.22	197	1.6%	2.56 [1.85, 3.27]
Qian GQ [42]	0.36	0.24	9	0.26	0.22	82	4.5%	0.10 [-0.06, 0.26]
Chen X [43]	0.44	0.36	50	0.29	0.26	212	4.8%	0.15 [0.04, 0.26]
Zheng Y [44]	2.65	3.93	32	0.78	0.76	62	0.6%	1.87 [0.50, 3.24]
Zhou Y [46]	4.57	6.41	117	0.65	0.74	260	0.7%	3.92 [2.76, 5.08]
Bai X [47]	1.4	3.65	54	0.61	1.95	79	0.9%	0.79 [-0.27, 1.85]
Pei G [48]	0.9	0.57	133	0.63	0.58	144	4.7%	0.27 [0.13, 0.41]
Yao Q [49]	0.96	0.69	13	0.76	0.77	83	2.9%	0.20 [-0.21, 0.61]
Han M [51]	0.51	0.32	32	0.27	0.15	122	4.8%	0.24 [0.13, 0.35]
Deng Q [52]	22.7	37.2	67	0.93	0.99	45	0.0%	21.77 [12.86, 30.68]
Gong J [53]	1.2	0.82	28	0.99	0.59	161	3.5%	0.21 [-0.11, 0.53]
Total (95% CI)			**1499**			**4882**	**100.0%**	**0.45 [0.34, 0.56]**

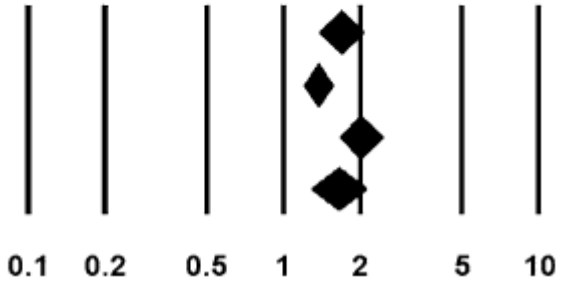
Heterogeneity: Tau² = 0.06; Chi² = 258.28, df = 33 (P < 0.00001); I² = 87%
Test for overall effect: Z = 8.09 (P < 0.00001)

Sci Rep. 2021 Nov 8;11(1):21888. doi: 10.1038/s41598-021-01462-5.

D-dimer, disease severity, and deaths (3D-study) in patients with COVID-19: a systematic review and meta-analysis of 100 studies

Seshadri Reddy Varikasuvu [1], Saurabh Varshney [2], Naveen Dutt [3], Manne Munikumar [4], Shahir Asfahan [3], Paresh P Kulkarni [5], Pratima Gupta [6]

Group by Outcome Type	Statistics for each study				
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
CEP	1.674	1.376	2.037	5.151	0.000
Mortality	1.360	1.199	1.542	4.794	0.000
Severity	1.994	1.646	2.414	7.067	0.000
Overall	1.643	1.288	2.095	3.994	0.000



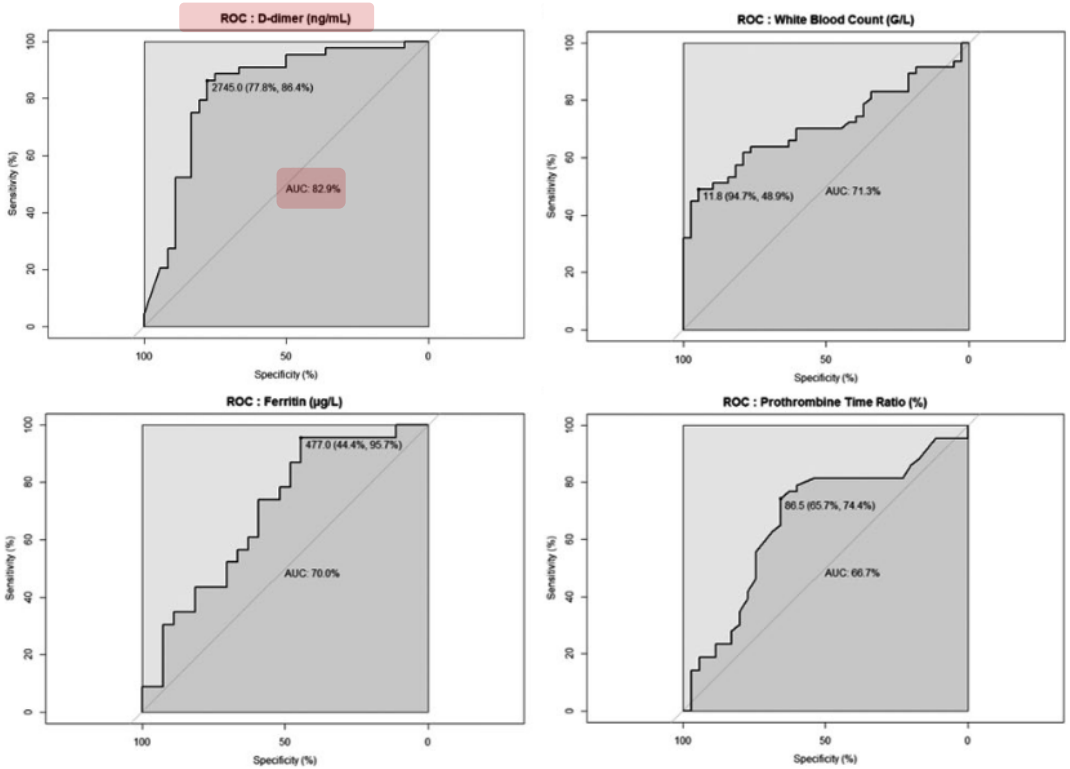
	Severity	Mortality	Overall-disease progression
Pooled Sensitivity	0.55	0.64	0.59
Pooled Specificity	0.56	0.66	0.62
AUC (SE)	0.69 (0.02)	0.79 (0.02)	0.75 (0.01)

Eur J Haematol. 2021 Aug;107(2):190-201

White blood count, D-dimers, and ferritin levels as predictive factors of pulmonary embolism suspected upon admission in noncritically ill COVID-19 patients: The French multicenter CLOTVID retrospective study

Lariboisière COVID Group

Variable	OR	95% CI	*P*-value
Obesity	0.2	0.04-0.7	.0152
Diabetes m[illegible]s	0.2	0.05-0.5	.0032
D-dimer ≥3000 ng/mL	18.5	6.4-61.5	<.0001
WBC ≥12 G/L	15.8	4.16-104.6	.0004
Ferritin ≥480 µg/L	17.6	3.0-338.1	.0087
Prothrombin time ratio >1.05	5.7	2.1-16.0	.0006



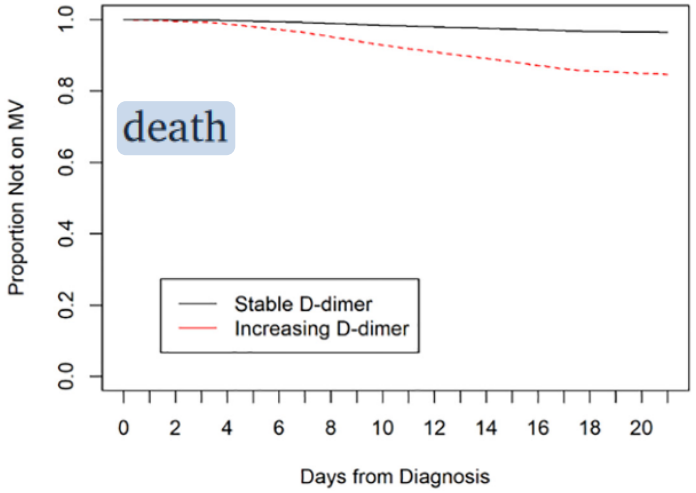
International Federation of Clinical Chemistry and Laboratory Medicine

Thrombosis Research 196 (2020) 99–105

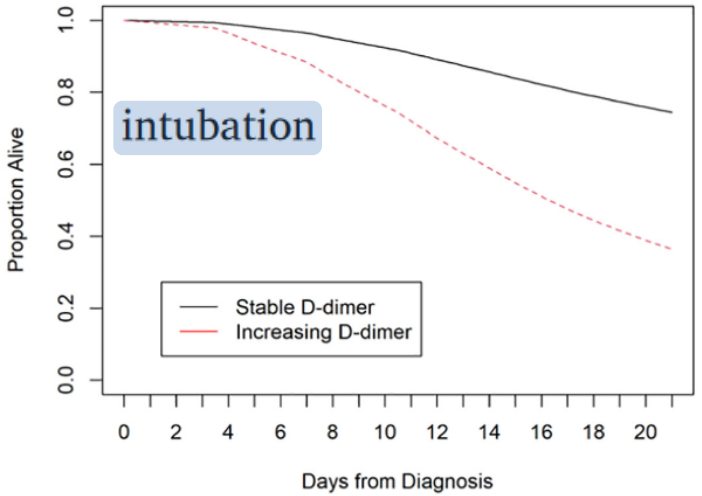
Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19

Leonard Naymagon[a,*], Nicole Zubizarreta[b], Jonathan Feld[a], Maaike van Gerwen[c,d], Mathilda Alsen[c], Santiago Thibaud[a], Alaina Kessler[a], Sangeetha Venugopal[a], Iman Makki[e], Qian Qin[a], Sirish Dharmapuri[a], Tomi Jun[a], Sheena Bhalla[a], Shana Berwick[a], Krina Christian[f], John Mascarenhas[a], Francine Dembitzer[f], Erin Moshier[b], Douglas Tremblay[a]

Cox Model						
			Unadjusted		Adjusted*	
D-dimer Trajectory Group	N Subjects (%)	N Events (%)	HR [95% CI]	P-value	HR [95% CI]	P-value
Stable D-dimer	200 (82.3%)	22 (11.0%)	0.20 [0.10; 0.42]	<0.0001	0.22 [0.10; 0.45]	0.0001
Increasing D-dimer	43 (17.7%)	22 (51.2%)	Reference		Reference	



Cox Model						
			Unadjusted		Adjusted*	
D-dimer Trajectory Group	N Subjects (%)	N Events (%)	HR [95% CI]	P-value	HR [95% CI]	P-value
Stable D-dimer	275 (74.4%)	41 (14.9%)	0.27 [0.17; 0.44]	<0.0001	0.29 [0.17; 0.49]	<0.0001
Increasing D-dimer	93 (25.2%)	45 (48.4%)	Reference		Reference	



Eur J Clin Invest. 2022 Jun 26;e13827. doi: 10.1111/eci.13827. Online ahead of print.

The Discrepancy between biomarkers of lung injury and 1-year mortality in COVID-19

Başak Atalay [1], Abdurrahman Cesur [2], Mehmet Agirbasli [3]

The predictors of one year mortality

	Sig.	Odds Ratio	95% C.I.for Odds Ratio	
			Lower	Upper
Age (years)	,530	1,017	,966	1,070
hs-CRP (mg/dl)	,805	1,006	,957	1,058
D-dimer (mg/dl)	,020	1,618	1,080	2,424
LDH (Units/L)	,264	1,003	,998	1,007
Troponin	,165	1,000	1,000	1,001
Ferritin	,141	1,000	1,000	1,001
Uric acid (mg/dl)	,141	1,261	,926	1,719
NLR	,147	1,053	,982	1,130
CT-SS	,383	,955	,862	1,059
GENDER	,985	,981	,137	7,028
Constant	,025	,001		

J Thromb Haemost. 2020 Sep;18(9):2408-2411

The need for accurate D-dimer reporting in COVID-19: Communication from the ISTH SSC on fibrinolysis

Jecko Thachil, Colin Longstaff, Emmanuel J. Favaloro, Giuseppe Lippi, Tetsumei Urano, Paul Y. Kim ✉, on behalf of the SSC Subcommittee on Fibrinolysis of the International Society on Thrombosis and Haemostasis

RECOMMENDATIONS

- The type of the of the D-dimer assay (name and manufacturer) must always be clearly reported
- The minimal analytical performance of the assay (including at least the functional sensitivity, total imprecision, linearity, and potential interference from FDPs) should be described
- A standardized measuring unit should be used for reporting data (FEU, as either "μg/L" or "mg/L")
- The cutoff value used in the study should be clearly indicated
- The statistical analysis should be appropriately selected according to sample size and value distribution (normal or not)

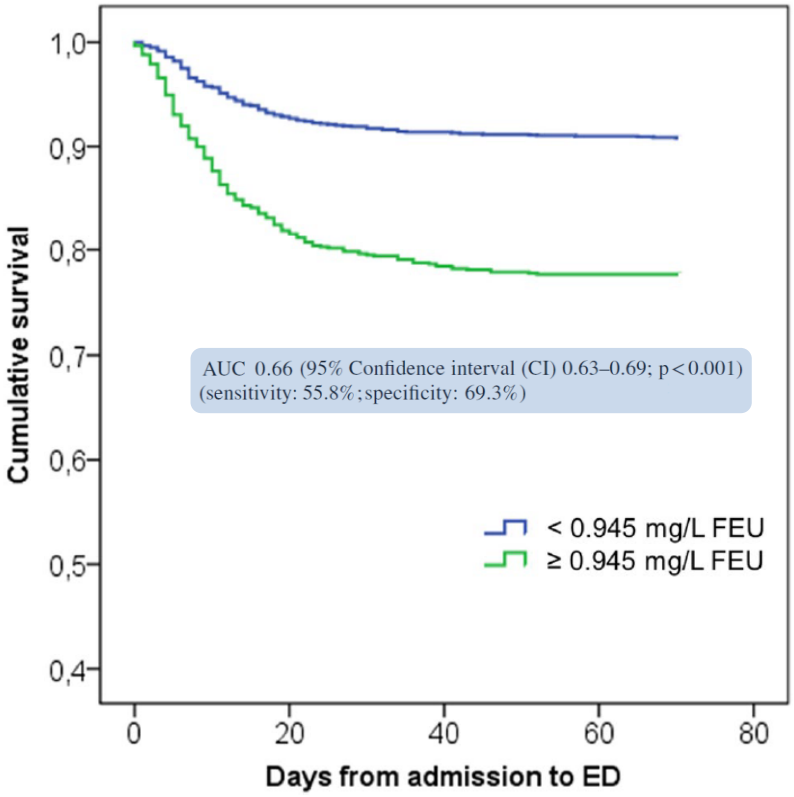
J Thromb Thrombolysis. 2021 Jul 16. doi: 10.1007/s11239-021-02527-y. Online ahead of print.

Harmonized D-dimer levels upon admission for prognosis of COVID-19 severity: Results from a Spanish multicenter registry (BIOCOVID-Spain study)

Luis García de Guadiana-Romualdo [# 1], Daniel Morell-García [# 2], Emmanuel J Favaloro [3],

Assay	Units[a]	Cut-off value	n (%)
Siemens Innovance® D-dimer	mg/L FEU	0.5 mg/L	513 (19.3)
Stago STA Liatest D-Di	µg/mL FEU	0.5 µg/mL	211 (7.9)
HemosIL D-Dimer HS	ng/mL DDU	230 ng/mL	324 (12.2)
HemosIL D-Dimer HS-500	ng/mL FEU	500 ng/mL	1615 (60.6

Assay[a]	Pool 1	Pool 2	Pool 3	Pool 4
Siemens Innovance® D-dimer ($y_m = 2.966\ x_m - 3.980$)	0.525	1.160	1.885	10.170
Stago STA Liatest D-Di ($y_m = 2.655\ x_m - 3.495$)	0.460	1.120	1.960	9.030
HemosIL D-Dimer HS ($y_m = 1.964\ x_m - 2.525$)	0.374	0.950	1.472	6.748
HemosIL D-Dimer HS-500 ($y_h = 2.197\ x_h - 2.843$)	0.393	1.075	1.582	7.542
Overall mean value	0.438	1.076	1.724	8.372

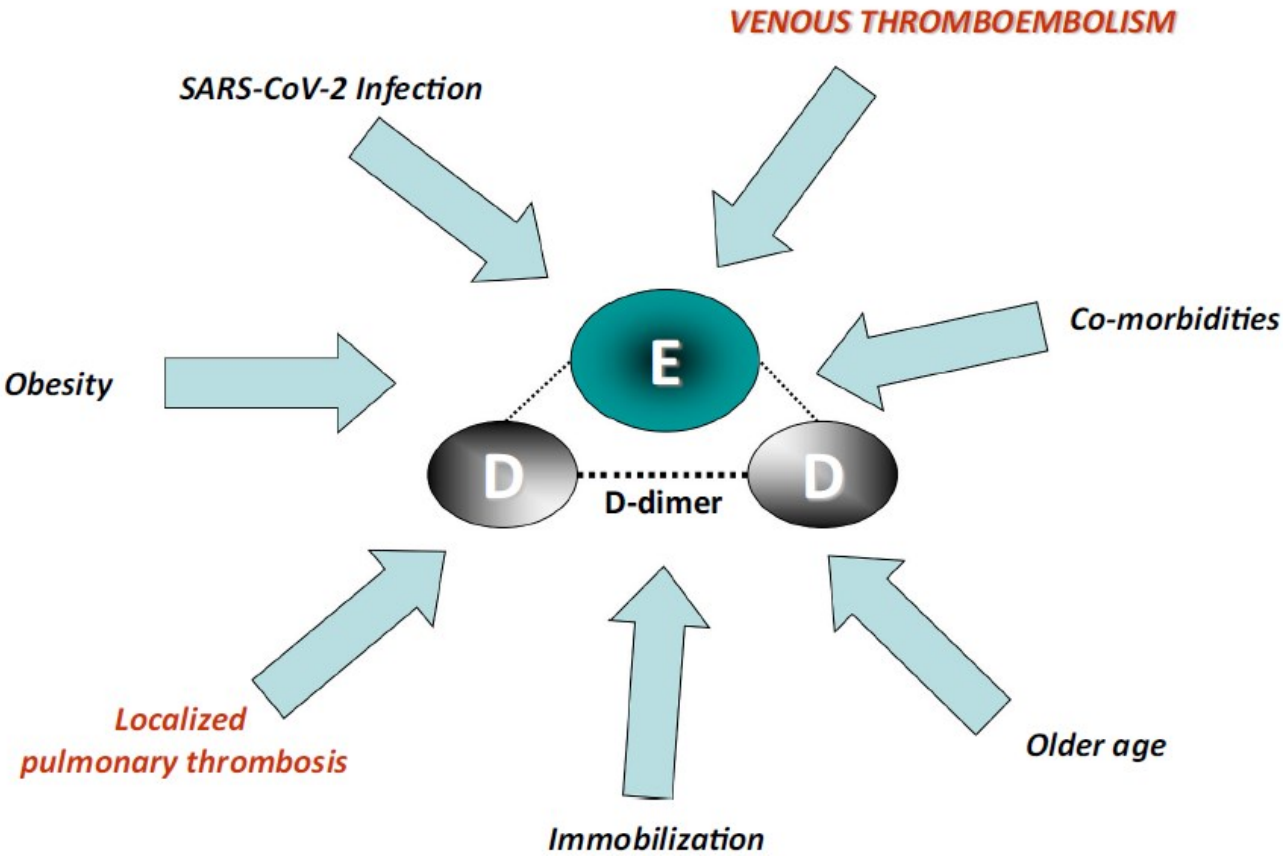


International Federation of Clinical Chemistry and Laboratory Medicine

Thrombosis Research 196 (2020) 635–637

D-dimer measurement in COVID-19: Silver bullet or clinical distraction?

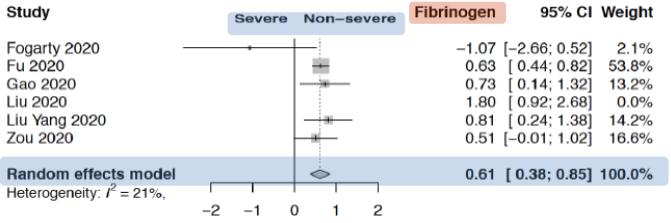
Giuseppe Lippi[a,*], Emmanuel J. Favaloro[b]

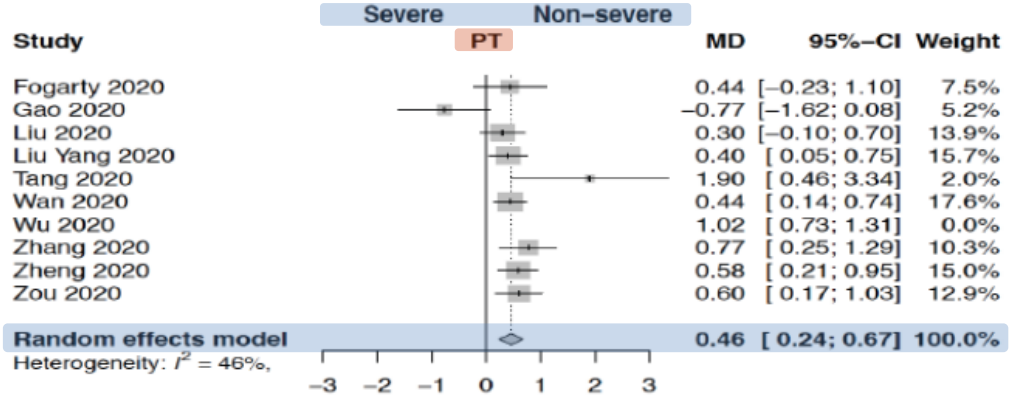


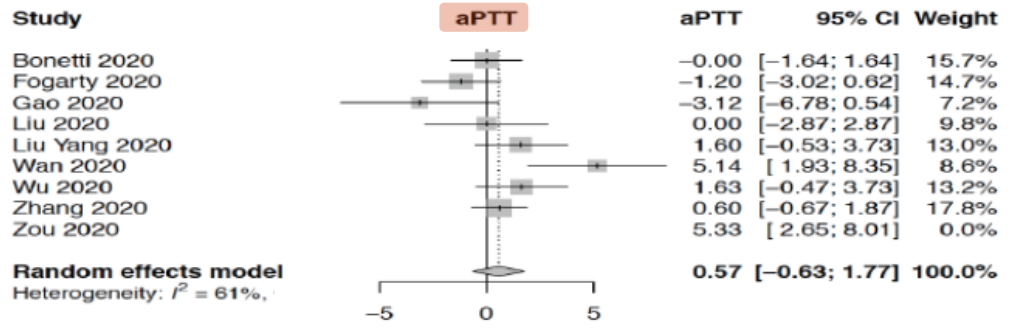
Ann Acad Med Singap. 2021 Apr;50(4):325-335

Severe COVID-19 and coagulopathy: A systematic review and meta-analysis

Saikat Mitra [1], Ryan Ruiyang Ling, Isabelle Xiaorui Yang, Wynne Hsing Poon, Chuen Seng Tan, Paul Monagle, Graeme MacLaren, Kollengode Ramanathan



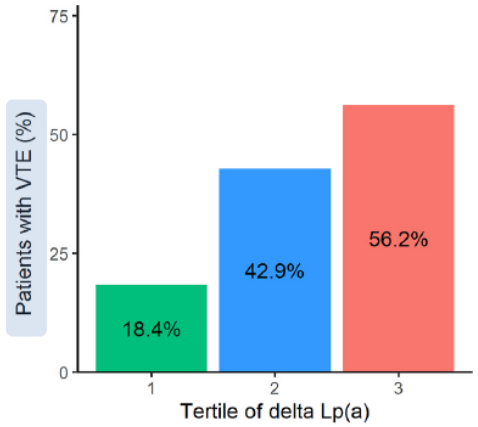


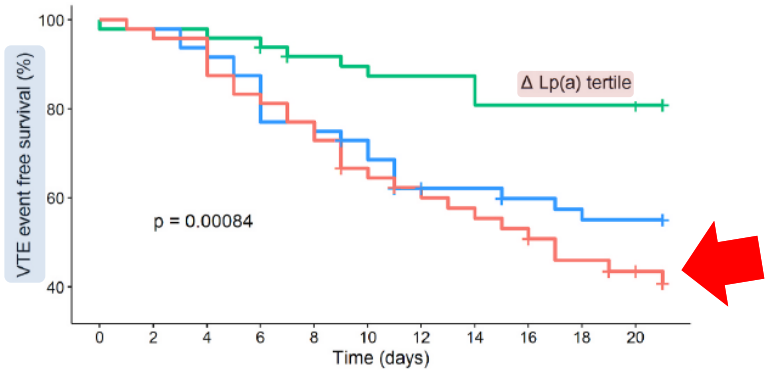


Atherosclerosis 341 (2022) 43–49

Lipoprotein(a), venous thromboembolism and COVID-19: A pilot study

Nick S. Nurmohamed[a,b], Didier Collard[a], Laurens F. Reeskamp[a], Yannick Kaiser[a], Jeffrey Kroon[c], Tycho R. Tromp[a], Amsterdam UMC Covid-19 Biobank, Bert-Jan H. van den Born[a], Michiel Coppens[a], Alexander P.J. Vlaar[d], Martijn Beudel[e], Diederik van de Beek[e], Nick van Es[a], Patrick M. Moriarty[f], Sotirios Tsimikas[g], Erik S. G. Stroes[a,*]





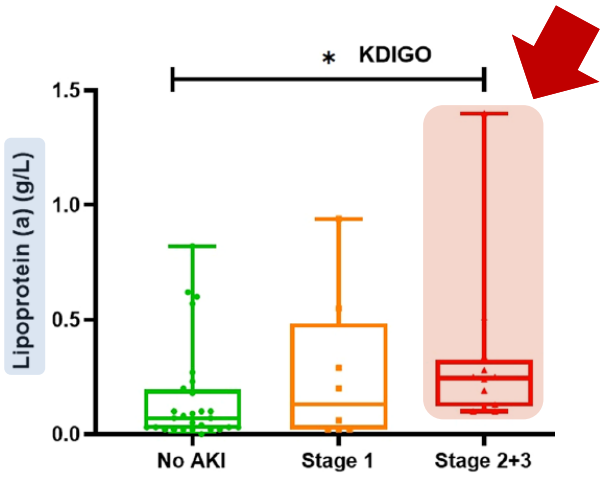
J Thromb Thrombolysis. 2021 Oct 28;1-5. doi: 10.1007/s11239-021-02597-y. Online ahead of print.

The role of lipoprotein(a) in coronavirus disease 2019 (COVID-19) with relation to development of severe acute kidney injury

Giuseppe Lippi[1] · Ivan Szergyuk[2] · Maria Helena Santos de Oliveira[3] · Stefanie W. Benoit[4,5] · Justin L. Benoit[6] · Emmanuel J. Favaloro[7] · Brandon Michael Henry[8,9]

Serum Lp(a) levels were significantly correlated with:

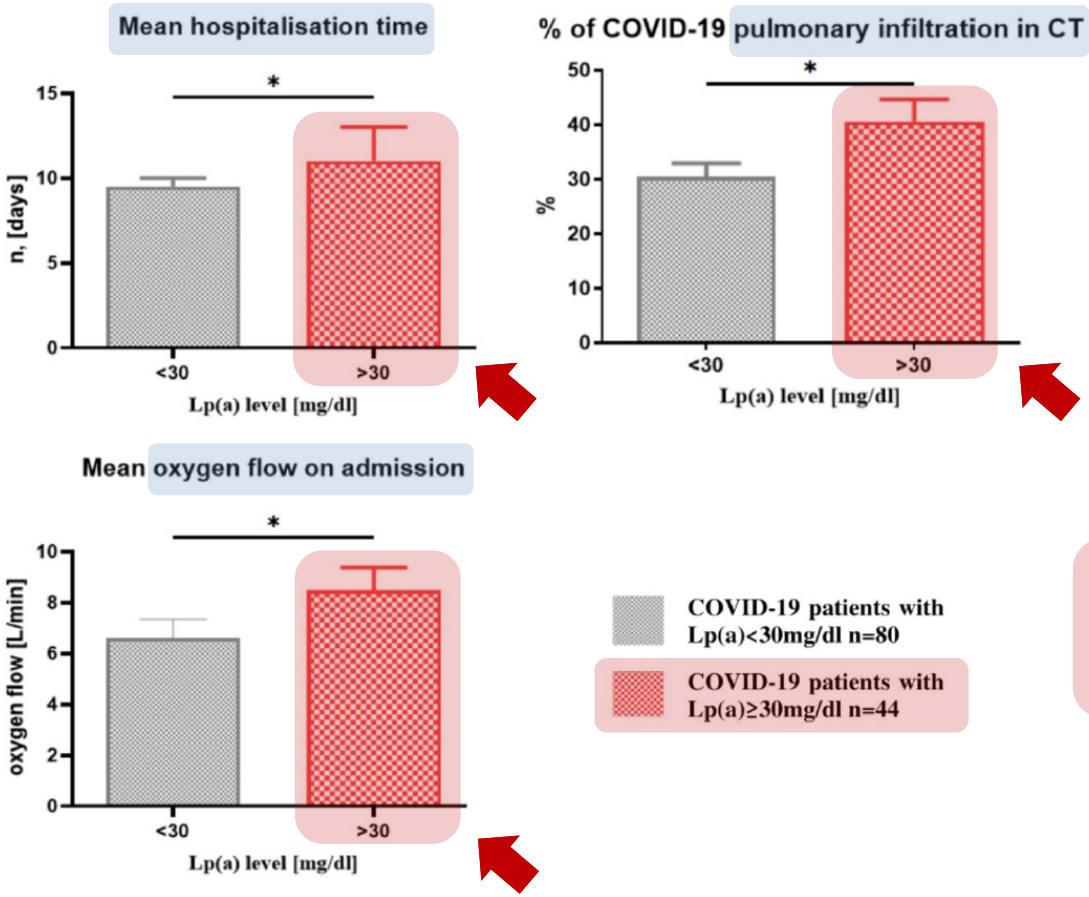
- ✓ Admission disease severity (r=0.355; p=0.013)
- ✓ Peak disease severity (r=0.314; p=0.03).



PLoS One. 2022 Jun 8;17(6):e0266814. doi: 10.1371/journal.pone.0266814. eCollection 2022.

Elevated Lp(a) and course of COVID–19: Is there a relationship?

Agnieszka Pawlos [1], Paulina Gorzelak-Pabiś [1], Mateusz Staciwa [1], Marlena Broncel [1]



Atherosclerosis. 2022 Mar 12;S0021-9150(22)00134-4. doi: 10.1016/j.atherosclerosis.2022.03.013.

Lipoprotein(a) in COVID-19: Genetics and inflammation collide

Martina Montagnana, Giuseppe Lippi *

Summary of clinical studies which explored the potential impact of lipoprotein(a) in the pathogenesis of COVID-19.

Authors	Study population	Conclusions
Nurmohamed et al., 2022 [5]	219 patients hospitalized with COVID-19	o Lp(a) variation significant correlated with concomitant changes of interleukin 6 o COVID-19 patients in the highest tertile of Lp(a) concentration had an over 3-fold risk of incident venous thromboembolism compared to those in the lowest tertile
Di Maio et al., 2022 [6]	428,453 control subjects recruited up to 2010 and 55, 199 subjects undergoing SARS-CoV-2 testing after March 2020 (13,588 with at least one positive test)	o In subjects with Lp(a) > 95th percentile the risk of ischemic heart disease was 5.3-fold higher in subjects with SARS-CoV-2 infection compared to those withou o In subjects with Lp(a) > 95th percentile the risk of venous thromboembolism was 3.9 higher in subjects with SARS-CoV-2 infection compared to those without
Lippi et al., 2021 [7]	50 patients with COVID-19 and 30 matched sick controls	o Serum Lp(a) values predicted incident peak COVID-19 severity

- ✓ Lp(a) values both at baseline (and thus presumably genetically determined) or during illness progression (and so boosted by COVID-19 related inflammation) have an impact on the clinical outcome of SARS-CoV-2 infection.
- ✓ Both baseline and serial Lp(a) assessment shall be part of a routine panel of laboratory tests for COVID-19 monitoring.

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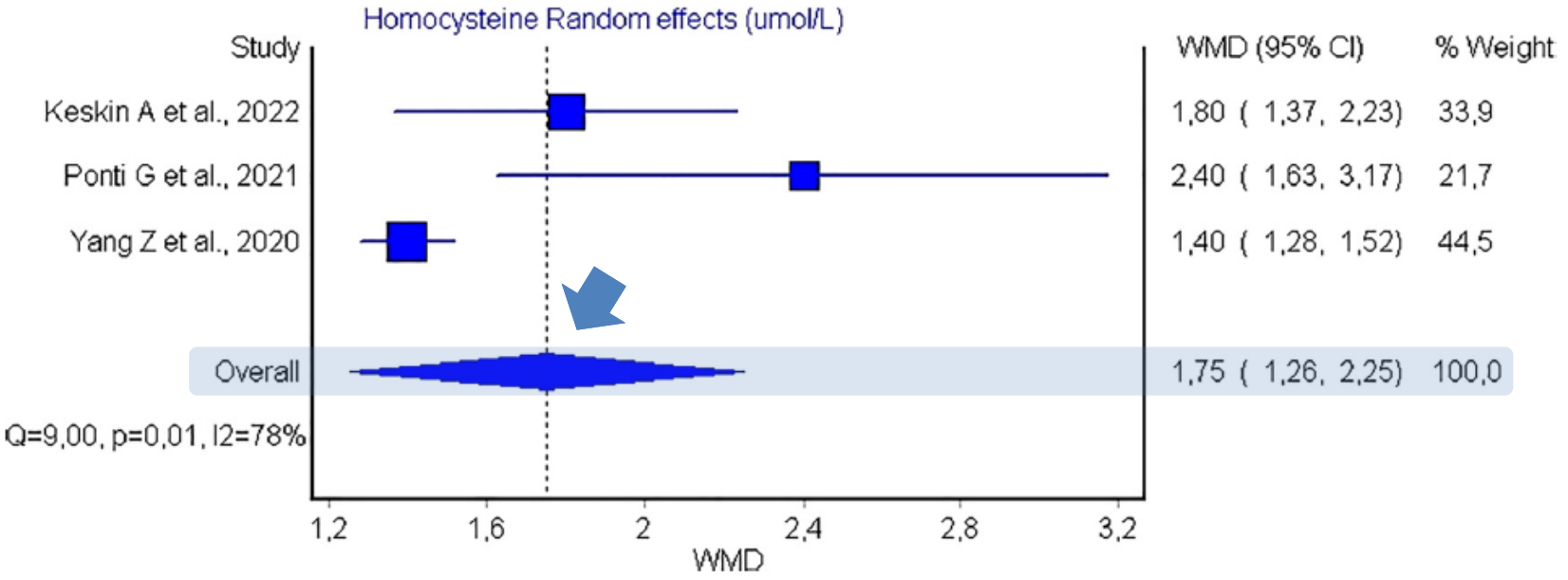
Homocysteine in coronavirus disease (COVID–19): a systematic literature review

Giovanni Carpenè [1], Davide Negrini [1], Brandon M Henry [2], Martina Montagnana [1], Giuseppe Lippi [1]

Weighted mean difference of Ln homocysteine values between COVID-19 patients with and without unfavorable outcome



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Recommendations for Minimal Laboratory Testing Panels in Patients with COVID-19: Potential for Prognostic Monitoring

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Test	Abbreviation	Rationale for inclusion	Considerations
Hematology (including hemostasis/coagulation)			
Complete/full blood count	CBC/FBC	Identification of lymphopenia, neutrophilia, and thrombocytopenia	Include platelet count, differential for lymphocyte count
Prothrombin Time	PT	Identification of ongoing coagulopathy	
Activated partial thromboplastin time	APTT		
Fibrinogen	Fbg or Fib	Identification of ongoing (consumption) coagulopathy	
D-dimer		Identification of ongoing (consumption or thrombotic) coagulopathy	[b]
Biochemistry and other tests			
Electrolytes		Identification of metabolic derangement	
Glucose			
C-reactive protein	CRP	Monitoring of infection/ inflammatory response	[b]
Lactate dehydrogenase	LDH	Identification of lung injury and/or multiple organ failure	
Aspartate aminotransferase	AST	Identification of liver injury	
Alanine aminotransferase	ALT		
Bilirubin			
Albumin		Identification of liver failure	
Creatine kinase (also known as creatine phosphokinase or phosphocreatine kinase)	CK	Identification of muscle injury	
Lipase		Identification of pancreatic injury	
blood urea nitrogen	BUN	Identification of kidney injury and/or failure	
Creatinine			
Cardiac biomarkers (troponin I or T)		Identification of cardiac injury	[b]
Brain natriuretic peptide	BNP	Identification of cardiac failure	[c]
Ferritin		Monitoring of infection/inflammatory response	[b]
Procalcitonin	PCT	Identification of bacterial coinfections	[b]
Presepsin		Monitoring of severity of viral infection	[d]