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THROMBOSIS, THROMBOPROPHYLAXIS AND COAGULOPATHY IN COVID- 19 INFECTIONS

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Coagulopathy of COVID-19

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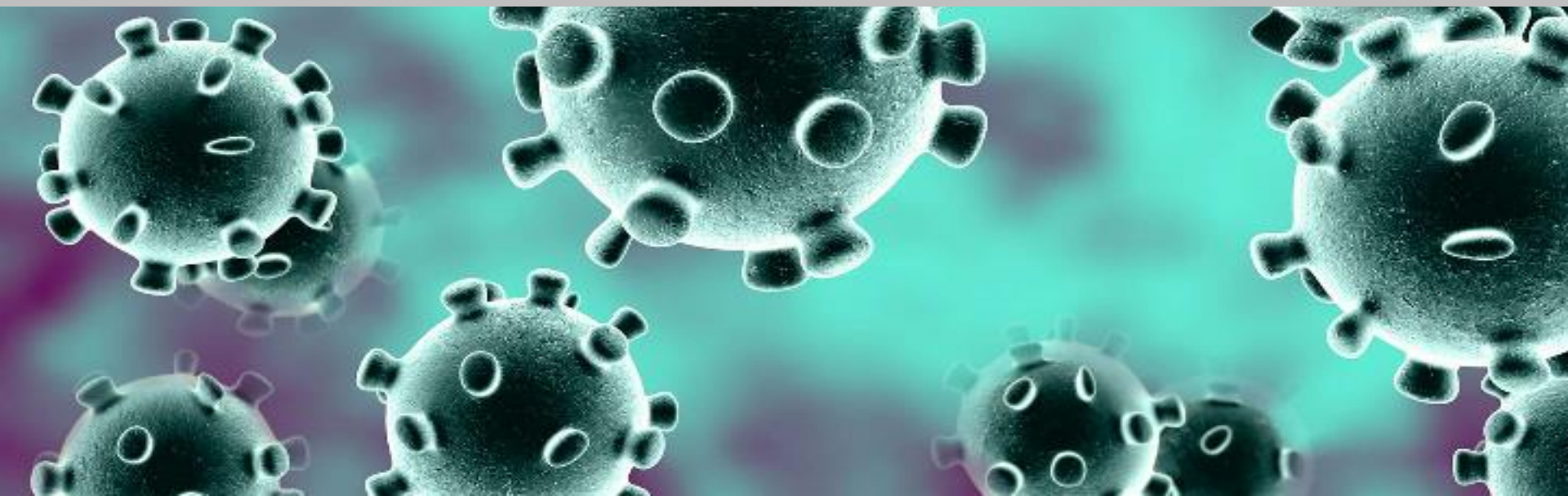


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Clinical Characteristics of Coronavirus Disease 2019 in China

W. Guan, Z. Ni, Yu Hu, W. Liang, C. Ou, J. He, L. Liu, H. Shan, C. Lei, D.S.C. Hui, B. Du, L. Li, G. Zeng, K.-Y. Yuen, R. Chen, C. Tang, T. Wang, P. Chen, J. Xiang, S. Li, Jin-lin Wang, Z. Liang, Y. Peng, L. Wei, Y. Liu, Ya-hua Hu, P. Peng, Jian-ming Wang, J. Liu, Z. Chen, G. Li, Z. Zheng, S. Qiu, J. Luo, C. Ye, S. Zhu, and N. Zhong, for the China Medical Treatment Expert Group for Covid-19*

This article was published on February 28, 2020, and last updated on March 6, 2020, at NEJM.org.

Clinical Characteristics of Coronavirus Disease 2019 in China

Variable	All Patients (N = 1099)	Disease Severity		Presence of Composite Primary End Point	
		Nonsevere (N = 926)	Severe (N = 173)	Yes (N = 67)	No (N = 1032)
Platelet count					
Median (IQR) — per mm^3	168,000 (132,000–207,000)	172,000 (139,000–212,000)	137,500 (99,000–179,500)	156,500 (114,200–195,000)	169,000 (133,000–207,000)
Distribution — no./total no. (%)					
<150,000 per mm^3	315/869 (36.2)	225/713 (31.6)	90/156 (57.7)	27/58 (46.6)	288/811 (35.5)
Median hemoglobin (IQR) — g/dl‡	13.4. (11.9–14.8)	13.5 (12.0–14.8)	12.8 (11.2–14.1)	12.5 (10.5–14.0)	13.4 (12.0–14.8)
D-dimer ≥0.5 mg/liter	260/560 (46.4)	195/451 (43.2)	65/109 (59.6)	34/49 (69.4)	226/511 (44.2)

Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

Fei Zhou, Ting Yu*, Ronghui Du*, Guohui Fan*, Ying Liu*, Zhibo Liu*, Jie Xiang*, Yeming Wang, Bin Song, Xiaoying Gu, Lulu Guan, Yuan Wei, Hui Li, Xudong Wu, Jiuyang Xu, Shengjin Tu, Yi Zhang, Hua Chen, Bin Cao*

	Non survivor (n=54)	Survivor (n=137)	
Lymphocytes < $0.8x10^9$/L	41 976%)	36 (26%)	<0.0001
Platelet count <$100x10^9$/L	1 (20%)	2 (1%)	<0.0001
LDH (IU)	521 (98%)	253 (54%)	<0.0001
Troponin I (> 28 pg/ml)	46%	1%	<0.0001
Prothrombin time (>16s)	13%	3%	-
Serum ferritin ug/L	1435 (96%)	503 (71%)	0.0008
IL-6 pg/ml	11 (7-14.5)	6.3 (5.0-7.9)	<0.0001
D Dimer >1 ug/ml	81%	24%	<0.0001

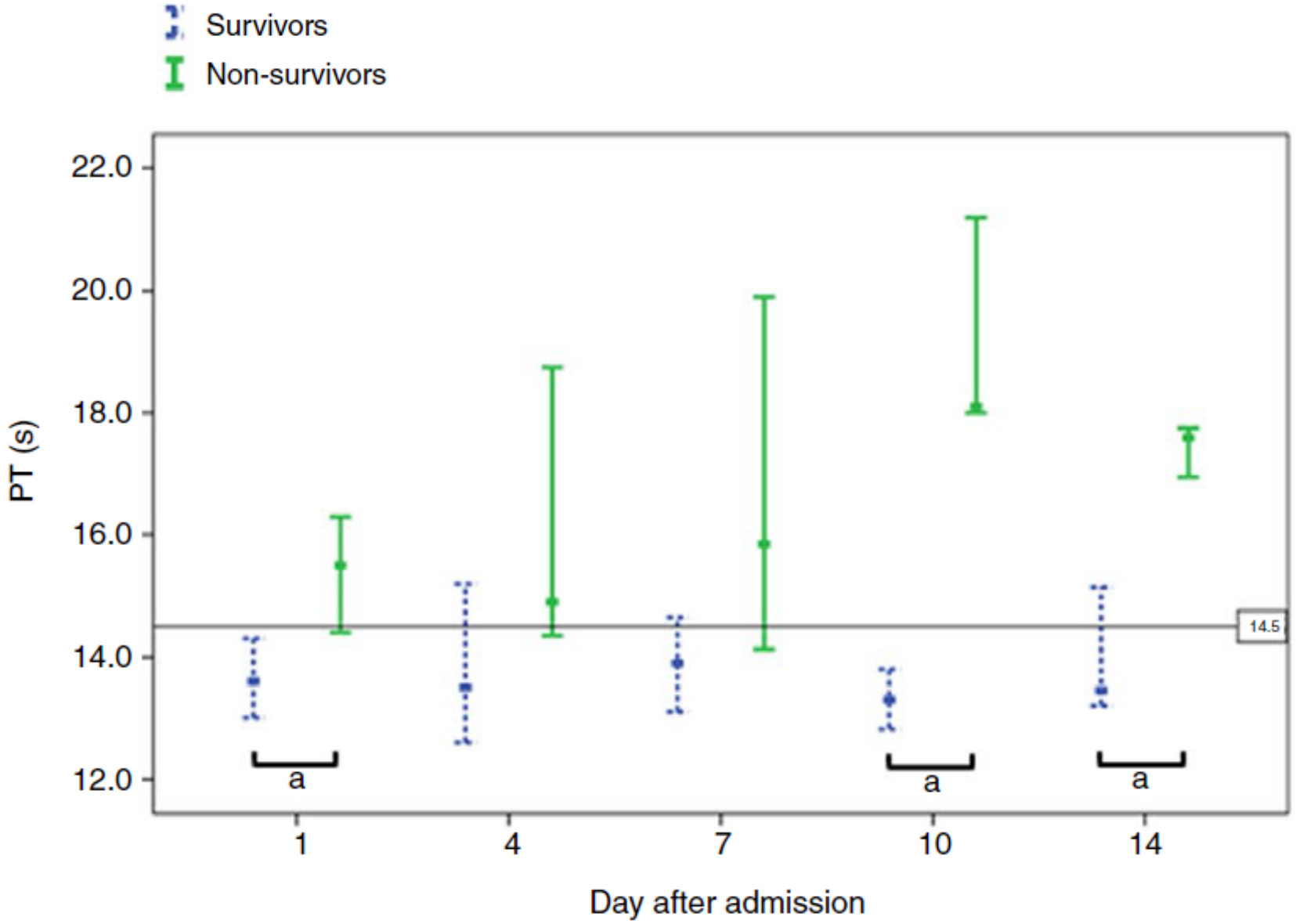
BRIEF REPORT

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]

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

J Thromb Haemost. 2020;18:844–847.



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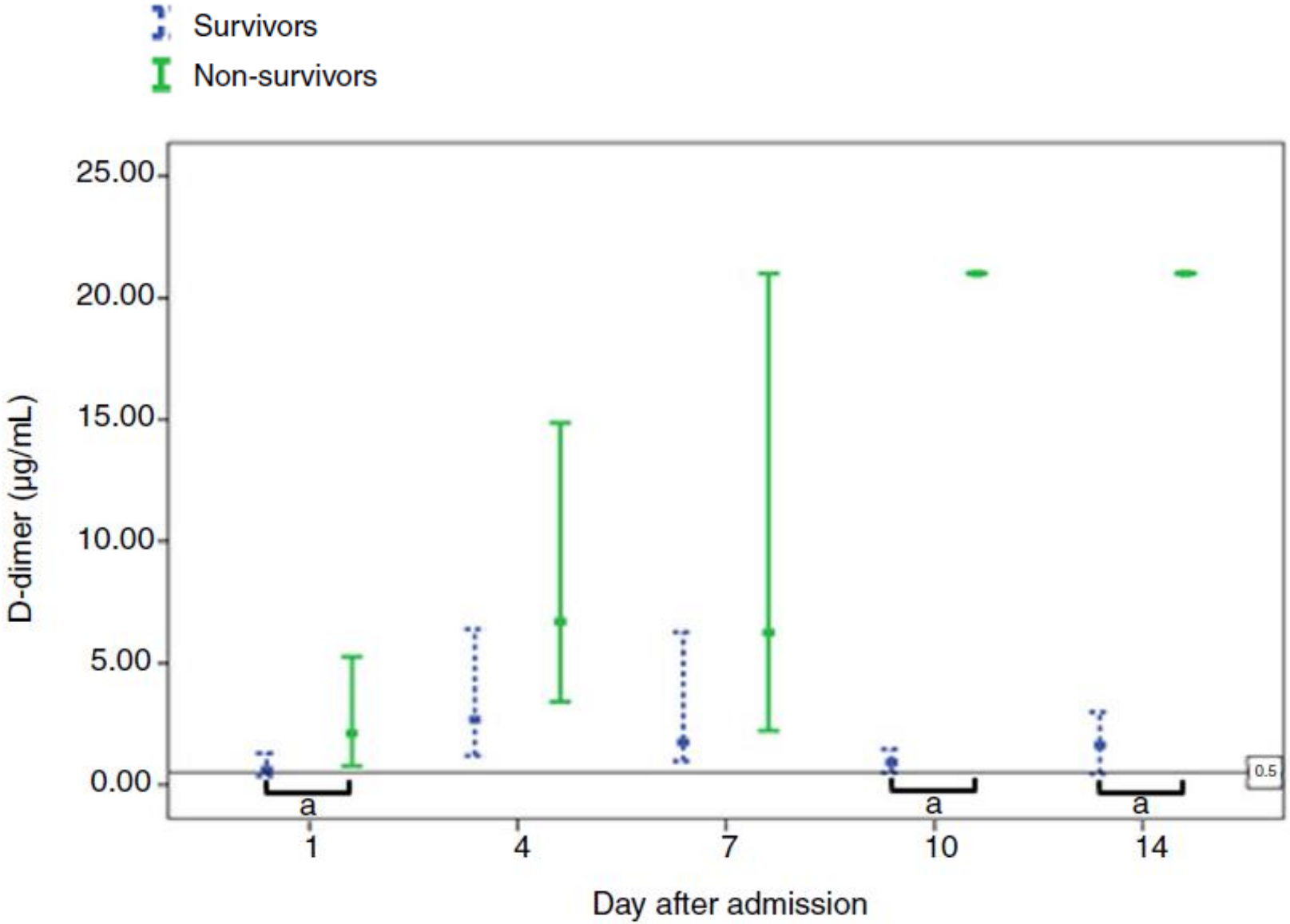

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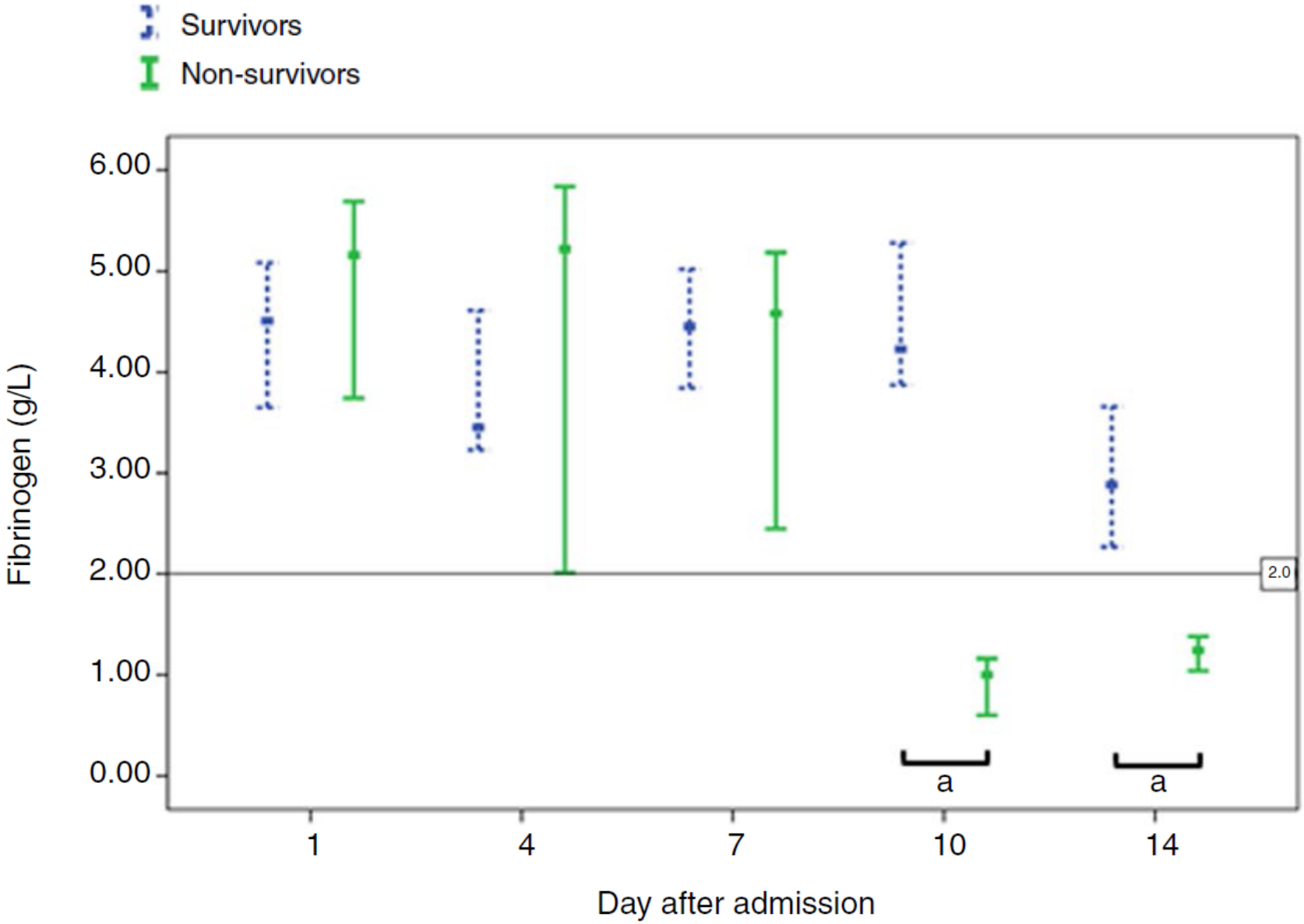
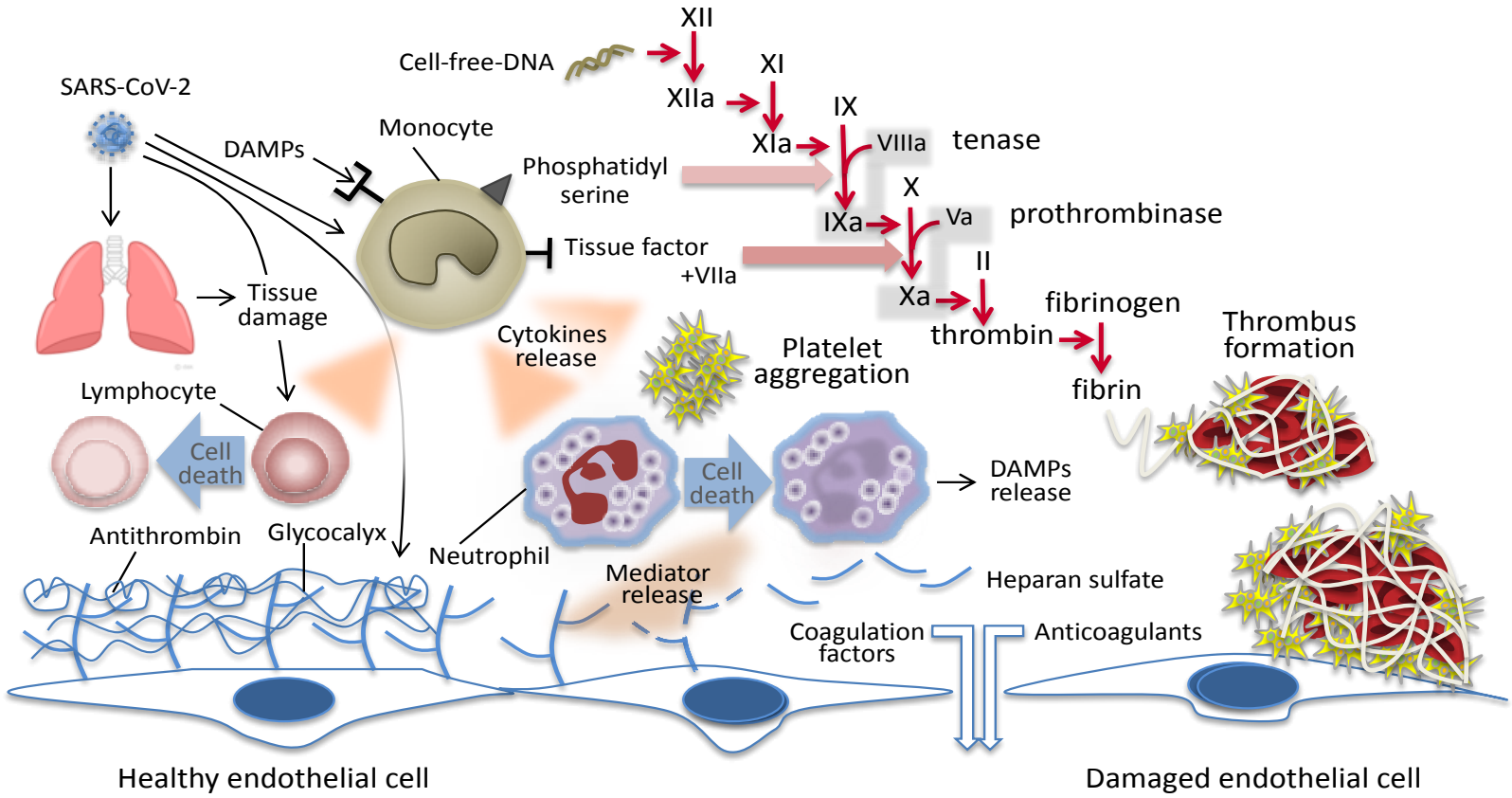


J Thromb Haemost. 2020;18:844–847.

COVID-19 coagulopathy: summary

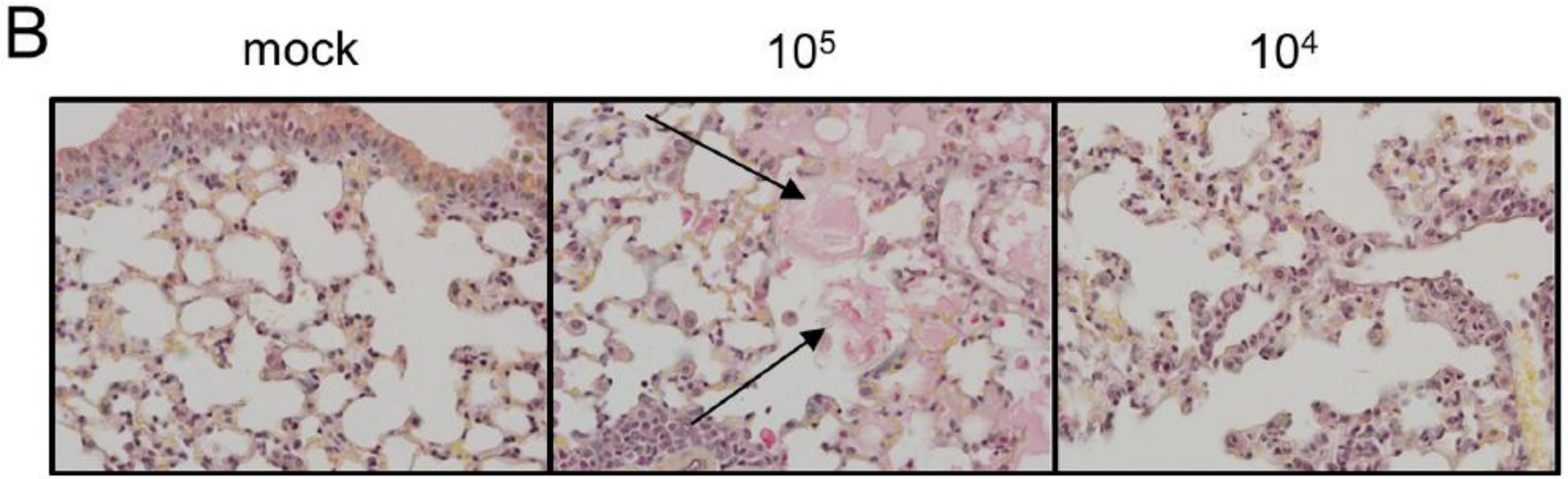
- Signs of coagulation activation mimicking DIC, but different from ‘usual’ sepsis-related DIC
  - Less prominent thrombocytopenia
  - Less consumption of coagulation proteins
- Clinical and pathological signs of thrombotic microangiopathy
  - vWF multimers and ADAMTS13 ?
- Prominent increase in D-dimer with predictive value for adverse outcome



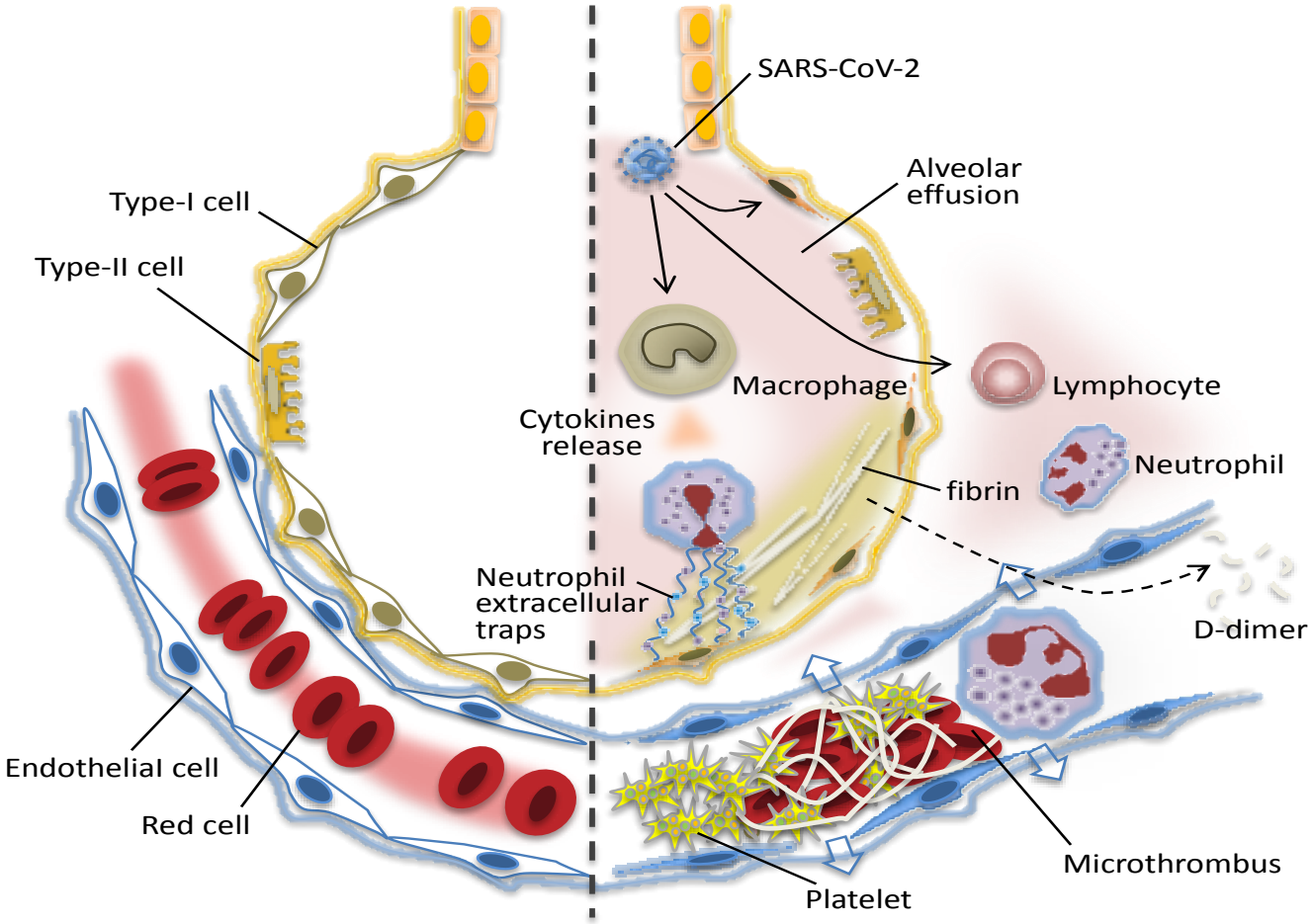
Iba T, et al, 2020

Mechanisms of Severe Acute Respiratory Syndrome Coronavirus-Induced Acute Lung Injury

Lisa E. Gralinski,[a] Armand Bankhead III,[b] Sophia Jeng,[b] Vineet D. Menachery,[a] Sean Proll,[c] Sarah E. Belisle,[c] Melissa Matzke,[d] Bobbie-Jo M. Webb-Robertson,[d] Maria L. Luna,[d] Anil K. Shukla,[d] Martin T. Ferris,[e] Meagan Bolles,[f] Jean Chang,[c] Lauri Aicher,[c] Katrina M. Waters,[d] Richard D. Smith,[d] Thomas O. Metz,[d] G. Lynn Law,[c] Michael G. Katze,[c,g] Shannon McWeeney,[b] Ralph S. Baric[a,f]



Plasminogen activator-driven pathways determine activation of the plasminogen-plasmin system and are an important factor in lethality



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Acute pulmonary embolism and COVID-19 pneumonia: a random association?

Gian Battista Danzi [1]*, **Marco Loffi** [1], **Gianluca Galeazzi** [1], and **Elisa Gherbesi** [2]

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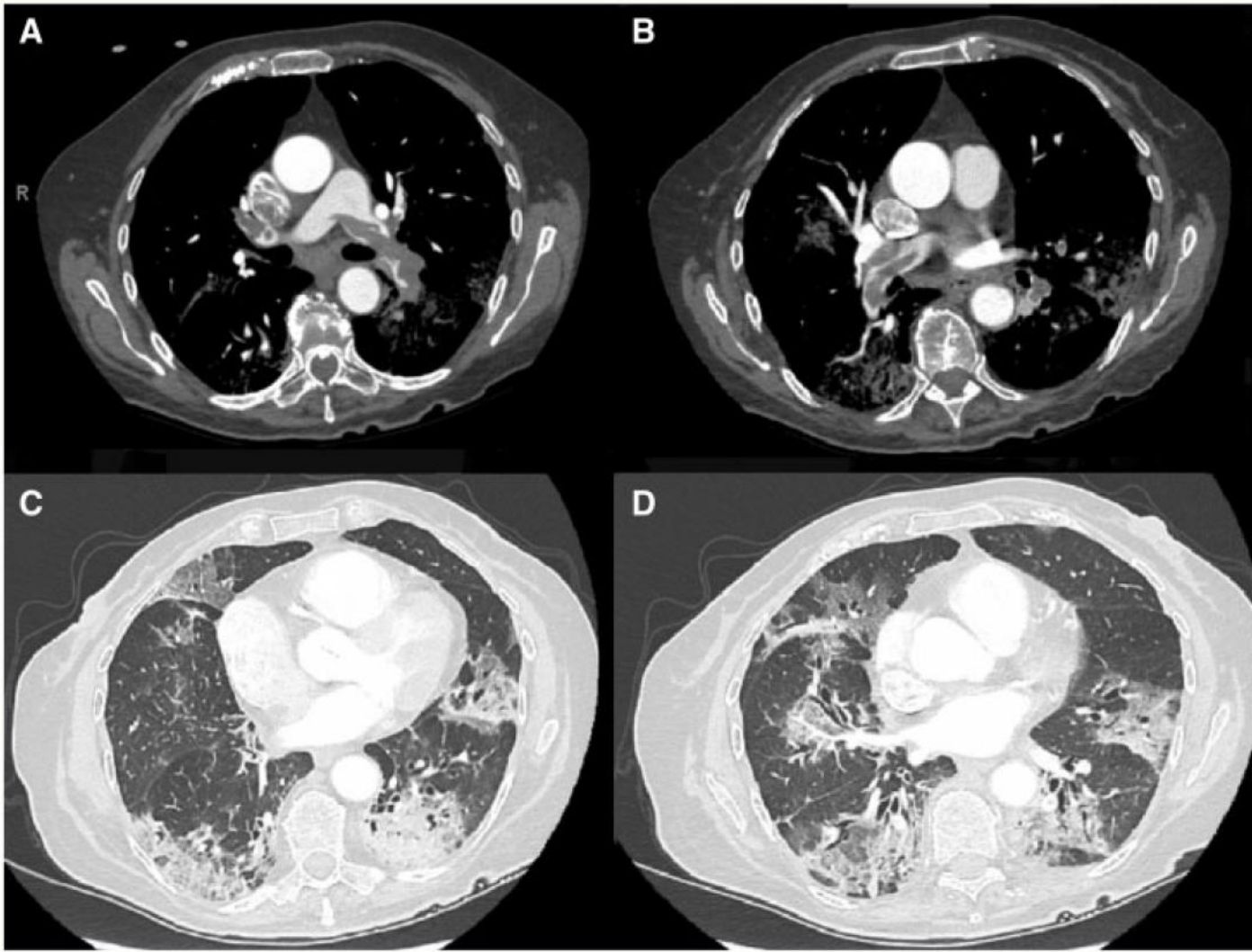
In a 75-year-old Covid-19-positive woman hospitalized for severe bilateral pneumonia, CT scan documented bilateral pulmonary embolism associated with extensive ground-glass opacifications involving both the lung parenchymas.

Acute infections are associated with a transient increased risk of venous thrombo-embolic events. A COVID-19-positive 75-year-old woman, with severe bilateral pneumonia and concomitant acute pulmonary embolism, was hospitalized after 10 days of fever and a recent onset of dyspnoea. She was haemodynamically stable and without strong predisposing risk factors for venous thrombo-embolism.



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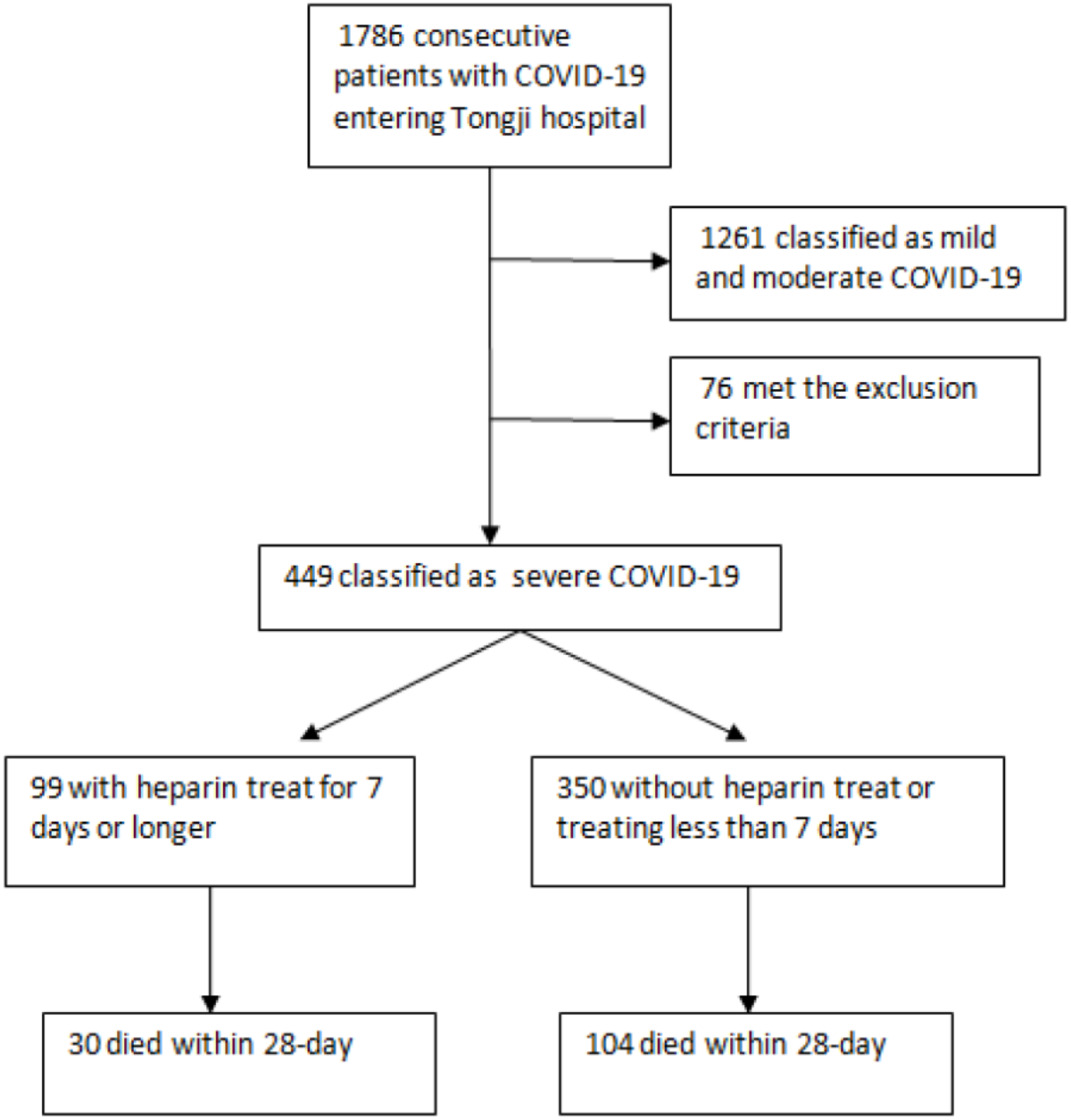
ORIGINAL ARTICLE | Free Access

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Ning Tang, Huan Bai, Xing Chen, Jiale Gong, Dengju Li, Ziyong Sun

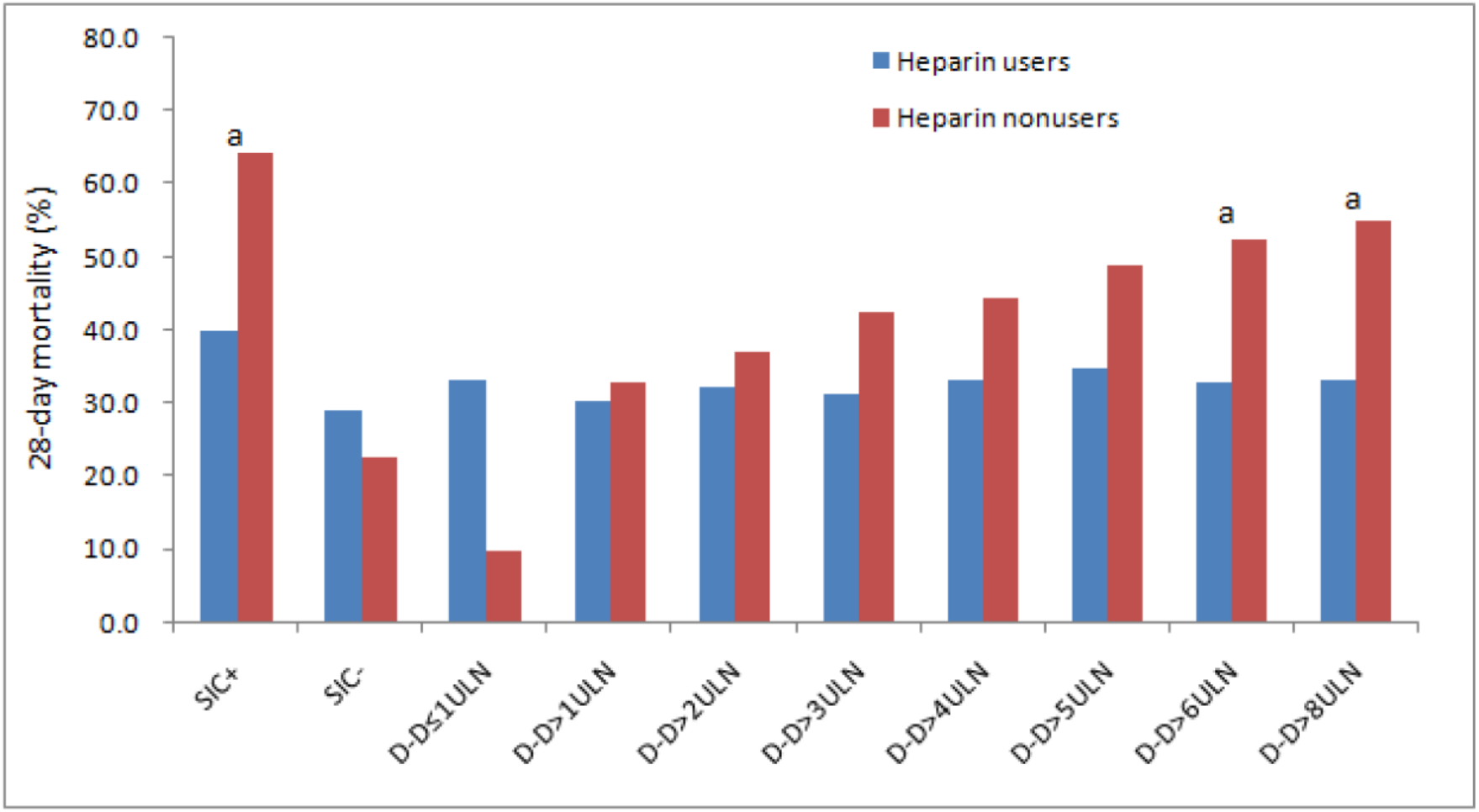
First published:27 March 2020 | https://doi.org/10.1111/jth.14817


1786 consecutive patients with COVID-19 entering Tongji hospital
1261 classified as mild and moderate COVID-19
76 met the exclusion criteria
449 classified as severe COVID-19
99 with heparin treat for 7 days or longer
350 without heparin treat or treating less than 7 days
30 died within 28-day
104 died within 28-day

Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy

Table 4 The association between heparin treatment and outcomes in stratified patients

Patients with	28-day mortality		Univariate analysis	
	Treating with Heparin	Non-treating with heparin	Odds ratio (95% CI)	*P* value
SIC socre≥4 (n=97)	40.0%	64.2%	0.372 (0.154-0.901)	0.029
SIC score≤4 (n=352)	29.0%	22.6%	1.284 (0.700-2.358)	0.419


80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
28-day mortality (%)
Heparin users
Heparin nonusers
a
a
a
SIC+
SIC-
D-D≤1ULN
D-D>1ULN
D-D>2ULN
D-D>3ULN
D-D>4ULN
D-D>5ULN
D-D>6ULN
D-D>8ULN

Conclusion

- Severe COVID-19 infection is associated with a coagulopathy with features of both DIC and thrombotic microangiopathy
- Coagulopathy is at least a marker of adverse outcome
- Severe COVID-19 seems to result in a pro-hemostatic state with possible consequences for the incidence of venous thromboembolism