Lancet :揭示新冠病毒肺炎致死危险因素

作者：任芳言 来源：科学网微信公号

本文原地址：https://www.iikx.com/news/topnews/8598.html

截至3月9日，意大利新冠肺炎死亡人数达463人。有观点称，该国死亡率增高与其老龄化程度有关。意大利目前因新冠病毒死亡的患者平均年龄81岁，且多数人有健康问题。

3月10日，中日友好医院副院长曹彬等人在《柳叶刀》刊发回顾性队列研究，指出高龄患者确实更可能面临死亡风险。

研究发现一些指标与死亡率密切相关，比如高龄、入院时器官衰竭评估(SOFA)分数较高，以及血栓标志物D-二聚体含量大于1微克/升等。

同时，研究人员首次关注了新冠病毒排毒时间，即病毒感染宿主细胞并继续繁殖的时间。研究显示，幸存者排毒持续时间的中位数为20天，最短8天，其中一例长达37天。

该文由北京协和医院、武汉金银潭医院、中日友好医院及清华药学院的研究者共同完成。

Articles

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*

Summary

Background Since December, 2019, Wuhan, China, has experienced an outbreak of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Epidemiological and clinical characteristics of patients with COVID-19 have been reported but risk factors for mortality and a detailed clinical course of illness, including viral shedding, have not been well described.

Methods In this retrospective, multicentre cohort study, we included all adult inpatients (≥18 years old) with laboratory-confirmed COVID-19 from Jinyintan Hospital and Wuhan Pulmonary Hospital (Wuhan, China) who had been discharged or had died by Jan 31, 2020. Demographic, clinical, treatment, and laboratory data, including serial samples for viral RNA detection, were extracted from electronic medical records and compared between survivors and non-survivors. We used univariable and multivariable logistic regression methods to explore the risk factors associated with in-hospital death.

Findings 191 patients (135 from Jinyintan Hospital and 56 from Wuhan Pulmonary Hospital) were included in this study, of whom 137 were discharged and 54 died in hospital. 91 (48%) patients had a comorbidity, with hypertension being the most common (58 [30%] patients), followed by diabetes (36 [19%] patients) and coronary heart disease (15 [8%] patients). Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1·10, 95% CI 1·03–1·17, per year increase; p=0·0043), higher Sequential Organ Failure Assessment (SOFA) score (5·65, 2·61–12·23; p<0·0001), and d-dimer greater than 1 μg/L (18·42, 2·64–128·55; p=0·0033) on admission. Median duration of viral shedding was 20·0 days (IQR 17·0–24·0) in survivors, but SARS-CoV-2 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days.

Published Online
March 9, 2020
https://doi.org/10.1016/
S0140-6736(20)30566-3

*Contributed equally

Department of Pulmonary and Critical Care Medicine, Center of Respiratory Medicine, National Clinical Research Center for Respiratory Diseases, Institute of Respiratory Medicine, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China (F Zhou MD, G Fan MS, Z Liu MD, Y Wang MD, X Gu PhD, H Li MD, Y Zhang MD, Prof B Cao MD); Department of Tuberculosis and Respiratory Disease (T Yu MD, Y Liu MD, B Song MS, Y Wei MS, S Tu MD, Prof H Chen MD) and Department of Clinical Laboratory (J Xiang MS), and GCP Center (X Wu MS), Jinyintan Hospital, Wuhan, China;

这些指标须警惕，有并发症者更危险

论文统计了191例患者的临床数据。他们全部来自武汉金银潭医院和武汉市肺科医院——武汉最早的两家定点医院。

入院时间在2019年12月至2020年1月。其中137人已出院，54人死亡。从疾病发生到出院的中位时间为22天，死亡中位时间为18.5天。

研究整理了191例病患的完整临床指标数据，发现死亡病患与幸存者间存在一系列指标差异。

比如年龄，死亡患者的年龄中位数为69岁，幸存者为52岁。

再比如SOFA评分，死亡患者的SOFA评分中位数为4.5，而幸存者评分中位数仅为1。

	Total (n=191)	Non-survivor (n=54)	Survivor (n=137)	p value
Demographics and clinical characteristics				
Age, years	56·0 (46·0–67·0)	69·0 (63·0–76·0)	52·0 (45·0–58·0)	<0·0001
Sex	..	..	..	0·15
Female	72 (38%)	16 (30%)	56 (41%)	..
Male	119 (62%)	38 (70%)	81 (59%)	..
Exposure history	73 (38%)	14 (26%)	59 (43%)	0·028
Current smoker	11 (6%)	5 (9%)	6 (4%)	0·21
Comorbidity	91 (48%)	36 (67%)	55 (40%)	0·0010
Hypertension	58 (30%)	26 (48%)	32 (23%)	0·0008
Diabetes	36 (19%)	17 (31%)	19 (14%)	0·0051
Coronary heart disease	15 (8%)	13 (24%)	2 (1%)	<0·0001
Chronic obstructive lung disease	6 (3%)	4 (7%)	2 (1%)	0·047
Carcinoma	2 (1%)	0	2 (1%)	0·37
Chronic kidney disease	2 (1%)	2 (4%)	0	0·024
Other	22 (12%)	11 (20%)	11 (8%)	0·016
Respiratory rate >24 breaths per min	56 (29%)	34 (63%)	22 (16%)	<0·0001
Pulse ≥125 beats per min	2 (1%)	2 (4%)	0	0·024
Systolic blood pressure <90 mm Hg	1 (1%)	0	1 (1%)	0·53
Fever (temperature ≥37·3°C)	180 (94%)	51 (94%)	129 (94%)	0·94
Cough	151 (79%)	39 (72%)	112 (82%)	0·15
Sputum	44 (23%)	14 (26%)	30 (22%)	0·55
Myalgia	29 (15%)	8 (15%)	21 (15%)	0·93
Fatigue	44 (23%)	15 (28%)	29 (21%)	0·33
Diarrhoea	9 (5%)	2 (4%)	7 (5%)	0·67
Nausea or vomiting	7 (4%)	3 (6%)	4 (3%)	0·40
SOFA score	2·0 (1·0–4·0)	4·5 (4·0–6·0)	1·0 (1·0–2·0)	<0·0001
qSOFA score	1·0 (0·0–1·0)	1·0 (1·0–1·0)	0·0 (0·0–1·0)	<0·0001
CURB-65 score	0·0 (0·0–2·0)	2·0 (1·0–3·0)	0·0 (0·0–1·0)	<0·0001
0–1	141/188 (75%)	16 (30%)	125/134 (93%)	<0·0001*
2	32/188 (17%)	23 (43%)	9/134 (7%)	..
3–5	15/188 (8%)	15 (28%)	0/134	..
Disease severity status	..	..	..	<0·0001
General	72 (38%)	0	72 (53%)	..
Severe	66 (35%)	12 (22%)	54 (39%)	..
Critical	53 (28%)	42 (78%)	11 (8%)	..
Time from illness onset to hospital admission, days	11·0 (8·0–14·0)	11·0 (8·0–15·0)	11·0 (8·0–13·0)	0·53

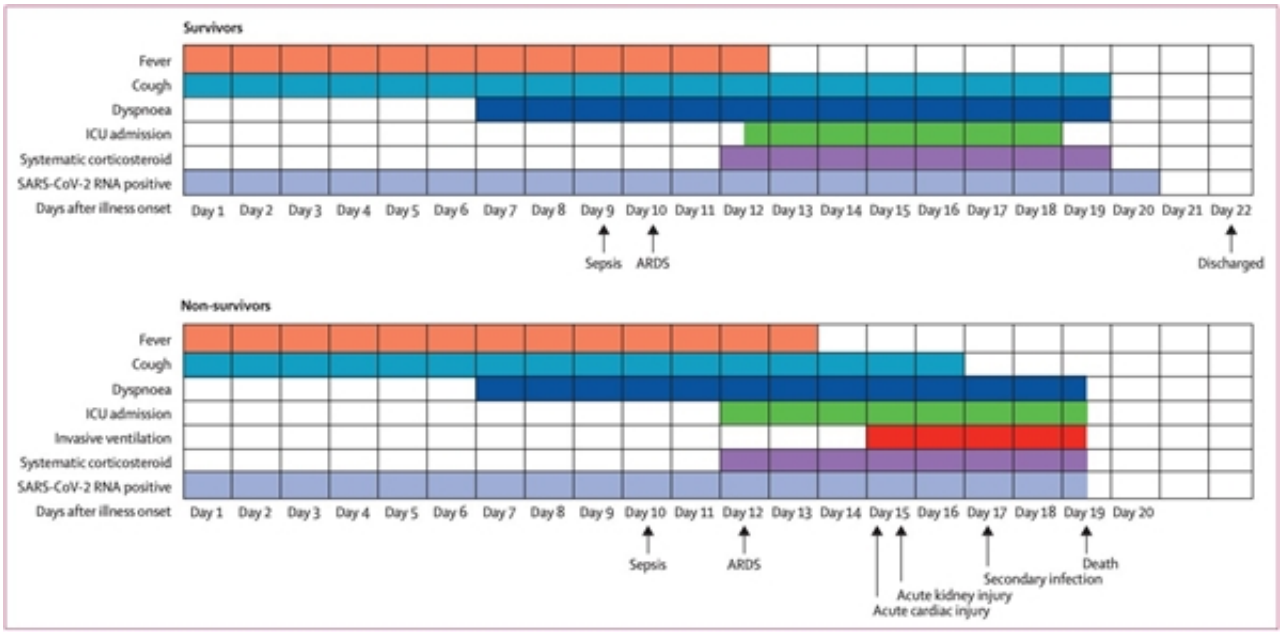
整个临床过程中，死亡病患的D-二聚体、铁蛋白、乳酸脱氢酶和白细胞介素-6(IL-6)等指标随疾病恶化有明显升高。发病后第16天，死亡病患的心肌钙蛋白I迅速增加，但幸存者这一指标在发病后第13天开始下降。

此外，住院期间，40%(77人)的患者出现淋巴细胞减少。幸存者的淋巴细胞计数会逐渐增多，而死亡病患的淋巴细胞持续减少，直至死亡。

与幸存者相比，死亡患者更易出现脓毒症、呼吸衰竭等并发症。半数死亡患者有继发性感染。幸存者和非幸存者使用皮质类固醇激素和静脉注射免疫球蛋白的表现有显著不同。单变量分析发现，患有糖尿病或冠心病等合并症的人死亡率更高。

关注病毒排毒期

病毒排毒期(viral shedding)
即病毒感染宿主细胞并继续繁殖的时间。在流感中，排毒期越长越可能导致死亡。文章指出，评估感染性病毒复制水平和持续时间，对评估病毒传播风险、制定治疗及隔离措施有重要意义。



住院患者主要症状、结局和病毒脱落持续时间。

曹彬等人此次统计的案例中，幸存者排毒持续时间的中位数为20天，而非幸存者一直到死亡当日，其病毒检测结果仍为阳性。

从发病起，幸存者中排毒期最短8天，其中一例长达37天。接受抗病毒治疗并出院的29例患者，从发病到开始接受治疗的中位时间较长，为14天，排毒期持续的中位时间为22天。重症患者排毒期持续时间为19天，危重患者为24天。

作者表示，病毒复制和排毒时间与病人预后直接相关，及时有效的抗病毒治疗对改变病人预后很关键。

目前，洛匹那韦和利托那韦及静脉注射瑞德西韦的随机临床实验仍在进行中。本研究统计的患者中，95%(181人)接受了抗生素治疗，21%(41人)接受洛匹那韦或利托那韦的抗病毒治疗。

为减少病毒复制、缩短病毒排毒时间，曹彬建议，应尽早开展抗病毒治疗、使用更有效的抗病毒药物，或采用两种及以上的有效药物联合治疗。“ 但这些都需要进一步研究探索。 ”曹彬在答复《柳叶刀》时表示。

参考资料：

https://interaktiv.morgenpost.de/corona-virus-karte-infektionen-deutschland-weltweit/?fbclid=IwAR04HlqzakGaNssQzbz4d8o8R3gz0C910U8tvfYlBT6P0lVJJvHfk9uS2rc

https://www.worldometers.info/coronavirus/country/italy/

https://doi.org/10.1016/S0140-6736(20)30566-3

https://mp.weixin.qq.com/s/grL0EDvNUA72VStOPu7fHA