Intensive Care Med (2020) 46:1472–1474
https://doi.org/10.1007/s00134-020-06047-w

LETTER

15-day mortality and associated risk factors for hospitalized patients with COVID-19 in Wuhan, China: an ambispective observational cohort study

Ke Wang[1,2], Zhiguo Zhang[3], Muqing Yu[1,2], Yu Tao[1,2] and Min Xie[1,2*]

Dear Editor,

An outbreak of COVID-19 has spread worldwide outside Wuhan, China [1]. It is urgent to evaluate the 15-day in-hospital mortality rate for this disease, and its associated risk factors [2].

For this single-center, ambispective cohort study of 548 patients [3], data at admission were retrospectively obtained. All the patients were followed up prospectively until day 15 after hospitalization. The primary endpoint of this study was death within 15 days of hospitalization. The risk factors for in-hospital mortality from COVID-19 were analyzed by means of multivariable Cox proportional hazards regression models.

Within 15 days of hospitalization, 78 patients died, resulting in mortality rates of around 14.2%. 127 patients were critically ill, i.e. needed ventilation support during the 15-day hospitalization. The risk of death within 15 days of admission was found to be higher in elderly male patients with a smoking history and underlying conditions such as chronic obstructive pulmonary disease, diabetes and hypertension (Supplementary Table 1). Compared with the survivors, the non-survivors more commonly presented the symptoms of dyspnea (88.5%), chest tightness (66.0%) and confusion (15.4%) (Supplementary Table 1). The non-survivors also presented with lower lymphocyte counts and higher levels of ferritin, lactate dehydrogenase (LDH) and C-reactive protein compared with the survivors (Supplementary Table 1). The majority of deaths were due to respiratory failure (88.5%), followed by cardiac arrest (5.1%) and shock (2.6%). Common complications among the death included acute respiratory distress syndrome (ARDS) (97.4%), hyperglycemia (67.9%), myocardial damage (62.8%), liver damage (24.4%), and renal damage (38.5%). Systemic glucocorticoid treatment was more common in non-survivors. Instead, more survivors than non-survivors received lopinavir/ritonavir and arbidol (33.4% vs. 9%, and 76.4% vs. 53.8%, respectively) (Supplementary Table 1).

Multivariable Cox proportional hazards regression showed that higher hazard ratios (HRs) for 15-day in-hospital death were associated with age older than 65 years, low oxygen saturation, lymphopenia, high LDH, and multiorgan dysfunction (Table 1). The most influential risk factor was severe lymphopenia ($< 0.5 \times 10^9$/L), which was associated with a higher hazard for mortality (HR = 4.410) compared with a lymphocyte count $> 0.5 \times 10^9$/L. The presence of multiorgan dysfunction increased the hazard (HR = 1.273, per organ increase). Treatment with lopinavir/ritonavirt (HR = 0.350) was associated with a lower hazard [4] (Table 1). Low-dose glucocorticoid treatment (< 1 mg/kg) or no glucocorticoid use was associated with a lower hazard compared with high-dose treatment (≥ 1 mg/kg) (Table 1). The risk factors for mortality in the critically ill patients are shown in Supplemental Table 2. However, in the critically ill cohort, the HR estimates were similar with and without systemic glucocorticoid

*Correspondence: xie_m@126.com
[1] Department of Pulmonary and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Wuhan 430030, China
Full author information is available at the end of the article
Ke Wang and Zhiguo Zhang have contributed equally to this work.

Table 1 Multivariable COX proportional risk regression modeling of risk factors for 15-day mortality in 548 inpatients

Variables	*B*	SE	Wald	*df*	Sig	Exp(*B*)	95.0% CI for Exp(*B*)	
							Lower	Upper
Age (> 65 year vs. ≤ 65)	0.674	0.257	6.847	1	0.009	1.962	1.184	3.249
SaO_2 (≥ = 93% vs. < 93%)	− 1.148	0.277	17.216	1	< 0.001	0.317	0.184	0.546
WBC count (reference > 10×10^9/L)			4.532	2	0.104			
< 4×10^9/L	− .355	0.494	0.516	1	0.472	0.701	0.266	1.846
4×10^9–10×10^9/L	− .589	0.277	4.531	1	0.033	0.555	0.323	0.954
Lymphocyte count (< 0.5×10^9/L vs. > 0.5×10^9/L)	1.484	0.595	6.23	1	0.013	4.41	1.375	14.143
LDH (reference ≥ 445 U/L)			20.608	2	< 0.001			
< 250 U/L	− 2.646	1.049	6.359	1	0.012	0.071	0.009	0.555
250–445 U/L	− 1.237	0.301	16.843	1	< 0.001	0.29	0.161	0.524
Multi-organ dysfunction	0.241	0.106	5.206	1	0.023	1.273	1.035	1.566
Lymphocyte * time	− 0.311	0.082	14.447	1	< 0.001	0.733	0.624	0.86
Treatment with glucocorticoid (reference ≥ 1 mg/kg)			8.198	2	0.017			
No	− 0.899	0.379	5.63	1	0.018	0.407	0.194	0.855
< 1 mg/Kg	− 0.644	0.277	5.395	1	0.02	0.525	0.305	0.904
Treatment with lopinavir/ritonavir (yes vs. no)	− 1.051	0.442	5.665	1	0.017	0.35	0.147	0.831
Treatment with arbidol (yes vs. no)	− 0.693	0.262	6.962	1	0.008	0.5	0.299	0.837
Treatment with ribavirin (yes vs. no)	0.353	0.386	0.84	1	0.36	1.424	0.669	3.033

P value (Sig.) < 0.05 from multivariable Cox regression analyses of the interactions terms between exposure variables was considered statistically significant

SaO_2 oxygen saturation, *WBC* white blood cell, *LDH* lactose dehydrogenase

therapy. This suggests glucocorticoid therapy requires strict control of indications [5]. The type of respiratory support (noninvasive vs. invasive ventilation) had no effect on mortality in critically ill patients (supplementary Table 2).

In conclusion, 14.2% patients of this cohort reached the primary endpoint of death within 15-day hospitalization. Aging, hypoxia, lymphopenia, high LDH level and multiple organ dysfunction were associated with increased 15-day in-hospital mortality from COVID-19. Lopinavir/ritonavir was associated with decreased mortality. Among the critically ill patients, the hazard ratio was not reduced in those receiving invasive ventilation versus non-invasive ventilation.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-020-06047-w) contains supplementary material, which is available to authorized users.

Author details

[1] Department of Pulmonary and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Wuhan 430030, China. [2] Key Laboratory of Respiratory Diseases, National Ministry of Health of the People's Republic of China and National Clinical Research Center for Respiratory Disease, Wuhan, China. [3] School of Medicine and Health Management, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Acknowledgements

We are indebted to Prof. Shuyun Xu and Prof. Min Zhou, who helped to conceive and design the study, and Drs. Ying Zhou, Jing Shi, Xiaochen Li, Bo Wu, Lu Qin, Zhenyu Yang, Cong Zhang and Junqing Yue for collecting cases or performing data analysis. We also thank Prof. Xiansheng Liu, Prof. Jungang Xie, and Prof. Jianping Zhao for scientific support. We respectfully and sincerely thank all front-line medical staff for their hard work and sacrifice.

Author contributions

MX conceived and designed the study. KW and MX contributed to the literature search and writing of the report. MY, KW and YT contributed to the data collection. MX, KW and ZZ contributed to the data analysis and data interpretation. KW and ZZ contributed equally and share first authorship.

Funding

This work was supported by grants from the Science and Technology Program of Hubei Province (2020FCA026). The funding source had no role in the design and conduct of the study, the analysis and interpretation of the data, or in the writing of the manuscript.

Compliance with ethical standards

Conflicts of interest

All authors declare no competing interests.

Ethical approval

This study was approved by the Ethics Commission of Tongji Hospital (TJ-C20200122).

Publisher's Note

Accepted: 8 April 2020
Published online: 23 April 2020

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