



Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19

Since December, 2019, the coronavirus disease 2019 (COVID-19) has spread globally, infecting more than 1 million people and causing more than 70 000 deaths.^{1,2} Among patients with COVID-19, especially those who are severely and critically ill, a variety of potential risk factors for venous thromboembolism exist, including infection, immobilisation, respiratory failure, mechanical ventilation, and central venous catheter use.^{3,4} However, to the best of our knowledge, risk of venous thromboembolism in these patients has not yet been reported. Here we use a nationwide dataset from China to provide a delineation of venous thromboembolism risk in patients with COVID-19.

On behalf of the National Clinical Research Centre for Respiratory Disease, together with the National Health Commission of the People's Republic of China, we collected data from 1099 patients with laboratory-confirmed COVID-19 in 31 provincial administrative regions throughout the country.⁵ The study was supported by the National Health Commission, was designed by the investigators, and was approved by the institutional review board of the National Health Commission. Written informed consent from the patients was waived in light of the urgent need to collect data, and the fact that this was a retrospective analysis of deidentified data. Data were analysed and interpreted by the authors. Continuous variables were expressed as medians with IQR. Wilcoxon rank-sum tests were applied to continuous variables, and χ^2 tests were used for categorical variables. To estimate the odds ratio (OR) associated with venous thromboembolism risk, variables including outcomes and laboratory findings that were adjusted by age (by use of logistic regression) were further analysed by logistic regression.

Venous thromboembolism risk was evaluated on admission to hospital via the Padua Prediction Score,⁶ data from 73 patients were excluded because of an absence of clinical information. Of the 1026 patients that were included, 407 (40%) were considered as high risk on the basis of a score of 4 or more—the remaining patients were defined as low risk. Bleeding risk was evaluated according to a published investigation,⁷ with patients considered to be at high risk if they had two or more

risk factors (aged 40 years or older, had hepatic failure (international normalised ratio >1.5), had severe renal failure (glomerular filtration rate <30 mL/min per m²), were admitted to the intensive care unit or the coronary care unit, had a central venous catheter, were diagnosed with a rheumatic disease or active cancer, or were men), or had one of the three major risk factors associated with bleeding: active gastroduodenal ulcer, bleeding in the 3 months before admission, or platelet count less than 50 × 10⁹/L. Patients at high risk of venous thromboembolism were older, and were more likely to have a high risk of bleeding, to have been admitted to the intensive care unit, to have had mechanical ventilation, and to have died as a result of COVID-19 or COVID-19 complications, such as venous thromboembolism, than patients at low risk of venous thromboembolism (table). Laboratory findings on admission showed that more patients with high risk of venous thromboembolism had abnormal concentrations of aspartate aminotransferase, alanine aminotransferase, and C-reactive protein than did patients with low risk after adjustment for age (appendix).

In patients with pneumonia caused by pneumococcal or influenza infection, the occurrence of venous thromboembolism has been shown to be increased.^{8,9} Although we do not know the number of patients with COVID-19 who had venous thromboembolism in this cohort, 40% of patients had a high risk, and an estimated 11% of high-risk patients go on to develop venous thromboembolism without prophylaxis.⁶ Most

Lancet Haematol 2020
Published Online
April 9, 2020
[https://doi.org/10.1016/S2352-3026\(20\)30109-5](https://doi.org/10.1016/S2352-3026(20)30109-5)

See Online for appendix

	Padua Prediction Score <4 (n=619)	Padua Prediction Score ≥4 (n=407)	OR (95% CI)*	p value*
High bleeding risk†	7 (1%)	44 (11%)	8.51 (3.74–19.35)	<0.0001
Intensive care unit admission	5 (1%)	47 (12%)	12.82 (5.00–32.91)	<0.0001
Mechanical ventilation	6 (1%)	57 (14%)	13.17 (5.56–31.19)	<0.0001
Mortality	0 (0%)	14 (3%)
Age, years	42 (33–55)	52 (40–64)	..	<0.0001
≥70‡	19 (3%) of 559	56 (15%) of 384	4.85 (2.83–8.31)	<0.0001

Data are n (%) or median (IQR). *Adjusted by age. †Bleeding risk was evaluated according to a previous study.⁷ ‡A threshold of 70 years was selected on the basis of the Padua Prediction Score and age data were not available for all patients.

Table: Bleeding score, outcomes, and age of patients with COVID-19 with high and low risk of venous thromboembolism according to the Padua Prediction Score

venous thromboembolism events can be prevented with appropriate prophylaxis, especially in high-risk patients. However, only ten (7%) of 140 patients for whom anticoagulation data were available in our cohort had received anticoagulant drugs during hospitalisation (nine were given heparin and one rivaroxaban)—a lower proportion than the proportion of patients at high risk of venous thromboembolism. This finding could suggest that venous thromboembolism prophylaxis was not adequate in this cohort of patients with COVID-19. Identifying patients with COVID-19 at high risk of venous thromboembolism and providing appropriate prophylaxis is therefore important.

Anticoagulant drugs are the cornerstone for venous thromboembolism prophylaxis; however, among the patients with COVID-19 at high risk of venous thromboembolism in this cohort, 44 (11%) of 407 also had a high risk of bleeding. For these patients, the dose and duration of anticoagulants should be adjusted, and mechanical compressions such as elastic compression stockings or intermittent pneumatic compression are warranted. Patients with COVID-19 can rapidly develop severe or critical disease, causing a series of complications such as renal failure, respiratory failure, or liver dysfunction,^{2,3,10} which can affect both venous thromboembolism and bleeding status. Therefore, assessing venous thromboembolism and bleeding risks regularly is essential. Additionally, we found that patients with COVID-19 with a high risk of venous thromboembolism had poorer outcomes than patients with a low risk, suggesting that these patients might require increased attention in case of rapid deterioration.

We declare no competing interests. TW, RC, and CL contributed equally.

Tao Wang, Ruchong Chen, Chunli Liu, Wenhua Liang, Weijie Guan, Ruidi Tang, Chunli Tang, Nuofu Zhang, Nanshan Zhong, *Shiyue Li
lishiyue@188.com

National Clinical Research Centre for Respiratory Disease, State Key Laboratory of Respiratory Disease, Guangzhou Institute of Respiratory Health, the First Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, 510120, China

- 1 Kim JY, Choe PG, Oh Y, et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: implication for infection prevention and control measures. *J Korean Med Sci* 2020; **35**: e61.
- 2 Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; published online Feb 24. DOI:10.1001/jama.2020.2648.
- 3 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; **323**: 1061–69.
- 4 Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395**: 507–13.
- 5 Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; published online Feb 28. DOI:10.1056/NEJMoa2002032.
- 6 Barber S, Noventa F, Rossetto V, et al. A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score. *J Thromb Haemost* 2010; **8**: 2450–57.
- 7 Kahn SR, Lim W, Dunn AS, et al. Prevention of VTE in nonsurgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; **141**(suppl 2): e195S–e226S.
- 8 Chen YG, Lin TY, Huang WY, Lin CL, Dai MS, Kao CH. Association between pneumococcal pneumonia and venous thromboembolism in hospitalized patients: a nationwide population-based study. *Respirology* 2015; **20**: 799–804.
- 9 Obi AT, Tignanelli CJ, Jacobs BN, et al. Empirical systemic anticoagulation is associated with decreased venous thromboembolism in critically ill influenza A H1N1 acute respiratory distress syndrome patients. *J Vasc Surg Venous Lymphat Disord* 2019; **7**: 317–24.
- 10 Kui L, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl)* 2020; published online Feb 7. DOI:10.1097/CM9.0000000000000744.