

World Journal of *Clinical Cases*

World J Clin Cases 2020 October 6; 8(19): 4280-4687



OPINION REVIEW

- 4280 Role of monoclonal antibody drugs in the treatment of COVID-19
Ucciferri C, Vecchiet J, Falasca K

MINIREVIEWS

- 4286 Review of simulation model for education of point-of-care ultrasound using easy-to-make tools
Shin KC, Ha YR, Lee SJ, Ahn JH
- 4303 Liver injury in COVID-19: A minireview
Zhao JN, Fan Y, Wu SD

ORIGINAL ARTICLE**Case Control Study**

- 4311 Transanal minimally invasive surgery *vs* endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: A retrospective analysis
Shen JM, Zhao JY, Ye T, Gong LF, Wang HP, Chen WJ, Cai YK
- 4320 Impact of *mTOR* gene polymorphisms and gene-tea interaction on susceptibility to tuberculosis
Wang M, Ma SJ, Wu XY, Zhang X, Abesig J, Xiao ZH, Huang X, Yan HP, Wang J, Chen MS, Tan HZ

Retrospective Cohort Study

- 4331 Establishment and validation of a nomogram to predict the risk of ovarian metastasis in gastric cancer: Based on a large cohort
Li SQ, Zhang KC, Li JY, Liang WQ, Gao YH, Qiao Z, Xi HQ, Chen L

Retrospective Study

- 4342 Predictive factors for early clinical response in community-onset *Escherichia coli* urinary tract infection and effects of initial antibiotic treatment on early clinical response
Kim YJ, Lee JM, Lee JH
- 4349 Managing acute appendicitis during the COVID-19 pandemic in Jiaxing, China
Zhou Y, Cen LS
- 4360 Clinical application of combined detection of SARS-CoV-2-specific antibody and nucleic acid
Meng QB, Peng JJ, Wei X, Yang JY, Li PC, Qu ZW, Xiong YF, Wu GJ, Hu ZM, Yu JC, Su W
- 4370 Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients
Wang L, He WB, Yu XM, Hu DL, Jiang H

- 4380 Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular carcinoma

Zhang YH, Su B, Sun P, Li RM, Peng XC, Cai J

- 4388 Clinical study on the surgical treatment of atypical Lisfranc joint complex injury

Li X, Jia LS, Li A, Xie X, Cui J, Li GL

- 4400 Application of medial column classification in treatment of intra-articular calcaneal fractures

Zheng G, Xia F, Yang S, Cui J

Clinical Trials Study

- 4410 Optimal hang time of enteral formula at standard room temperature and high temperature

Lakananurak N, Nalinthassanai N, Suansawang W, Panarat P

META-ANALYSIS

- 4416 Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer

Liu J, Wang Y, Yu Y

SCIENTOMETRICS

- 4431 Global analysis of daily new COVID-19 cases reveals many static-phase countries including the United States potentially with unstoppable epidemic

Long C, Fu XM, Fu ZF

CASE REPORT

- 4443 Left atrial appendage aneurysm: A case report

Belov DV, Moskalev VI, Garbuzenko DV, Arefyev NO

- 4450 Twenty-year survival after iterative surgery for metastatic renal cell carcinoma: A case report and review of literature

De Raffe E, Mirarchi M, Casadei R, Ricci C, Brunocilla E, Minni F

- 4466 Primary rhabdomyosarcoma: An extremely rare and aggressive variant of male breast cancer

Satală CB, Jung I, Bara TJ, Simu P, Simu I, Vlad M, Szodorai R, Gurzu S

- 4475 Bladder stones in a closed diverticulum caused by *Schistosoma mansoni*: A case report

Alkhamees MA

- 4481 Cutaneous ciliated cyst on the anterior neck in young women: A case report

Kim YH, Lee J

- 4488 Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high-dose combination cytotoxic chemotherapy: A case report

Kim HB, Lee HJ, Hong R, Park SG

- 4494** Acute amnesia during pregnancy due to bilateral fornix infarction: A case report
Cho MJ, Shin DI, Han MK, Yum KS
- 4499** Ascaris-mimicking common bile duct stone: A case report
Choi SY, Jo HE, Lee YN, Lee JE, Lee MH, Lim S, Yi BH
- 4505** Eight-year follow-up of locally advanced lymphoepithelioma-like carcinoma at upper urinary tract: A case report
Yang CH, Weng WC, Lin YS, Huang LH, Lu CH, Hsu CY, Ou YC, Tung MC
- 4512** Spontaneous resolution of idiopathic intestinal obstruction after pneumonia: A case report
Zhang BQ, Dai XY, Ye QY, Chang L, Wang ZW, Li XQ, Li YN
- 4521** Successful pregnancy after protective hemodialysis for chronic kidney disease: A case report
Wang ML, He YD, Yang HX, Chen Q
- 4527** Rapid remission of refractory synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome in response to the Janus kinase inhibitor tofacitinib: A case report
Li B, Li GW, Xue L, Chen YY
- 4535** Percutaneous fixation of neonatal humeral physal fracture: A case report and review of the literature
Tan W, Wang FH, Yao JH, Wu WP, Li YB, Ji YL, Qian YP
- 4544** Severe fundus lesions induced by ocular jellyfish stings: A case report
Zheng XY, Cheng DJ, Lian LH, Zhang RT, Yu XY
- 4550** Application of ozonated water for treatment of gastro-thoracic fistula after comprehensive esophageal squamous cell carcinoma therapy: A case report
Wu DD, Hao KN, Chen XJ, Li XM, He XF
- 4558** Germinomas of the basal ganglia and thalamus: Four case reports
Huang ZC, Dong Q, Song EP, Chen ZJ, Zhang JH, Hou B, Lu ZQ, Qin F
- 4565** Gastrointestinal bleeding caused by jejunal angiosarcoma: A case report
Hui YY, Zhu LP, Yang B, Zhang ZY, Zhang YJ, Chen X, Wang BM
- 4572** High expression of squamous cell carcinoma antigen in poorly differentiated adenocarcinoma of the stomach: A case report
Wang L, Huang L, Xi L, Zhang SC, Zhang JX
- 4579** Therapy-related acute promyelocytic leukemia with FMS-like tyrosine kinase 3-internal tandem duplication mutation in solitary bone plasmacytoma: A case report
Hong LL, Sheng XF, Zhuang HF
- 4588** Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report
Zhang X, Gu X, Li JG, Hu XJ

- 4595** Severe hyperlipemia-induced pseudoerythrocytosis - Implication for misdiagnosis and blood transfusion: A case report and literature review
Zhao XC, Ju B, Wei N, Ding J, Meng FJ, Zhao HG
- 4603** Novel brachytherapy drainage tube loaded with double 125I strands for hilar cholangiocarcinoma: A case report
Lei QY, Jiao DC, Han XW
- 4609** Resorption of upwardly displaced lumbar disk herniation after nonsurgical treatment: A case report
Wang Y, Liao SC, Dai GG, Jiang L
- 4615** Primary hepatic myelolipoma: A case report and review of the literature
Li KY, Wei AL, Li A
- 4624** Endoscopic palliative resection of a giant 26-cm esophageal tumor: A case report
Li Y, Guo LJ, Ma YC, Ye LS, Hu B
- 4633** Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review
Long X, Zhang L, Cheng Q, Chen Q, Chen XP
- 4644** Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report
Cai X, Yu JJ, Tian H, Shan ZF, Liu XY, Jia J
- 4652** Intravesically instilled gemcitabine-induced lung injury in a patient with invasive urothelial carcinoma: A case report
Zhou XM, Wu C, Gu X
- 4660** Bochdalek hernia masquerading as severe acute pancreatitis during the third trimester of pregnancy: A case report
Zou YZ, Yang JP, Zhou XJ, Li K, Li XM, Song CH
- 4667** Localized primary gastric amyloidosis: Three case reports
Liu XM, Di LJ, Zhu JX, Wu XL, Li HP, Wu HC, Tuo BG
- 4676** Displacement of peritoneal end of a shunt tube to pleural cavity: A case report
Liu J, Guo M
- 4681** Parathyroid adenoma combined with a rib tumor as the primary disease: A case report
Han L, Zhu XF

ABOUT COVER

Peer-reviewer of *World Journal of Clinical Cases*, Prof. Adrián Ángel Inchauspe, obtained his MD in 1986 from La Plata National University (Argentina), where he remained as Professor of Surgery. Study abroad, at the Aachen and Tübingen Universities in Germany in 1991, led to his certification in laparoscopic surgery, and at the Louis Pasteur University in Strasbourg France, led to his being awarded the Argentine National Invention Award in 1998 for his graduate work in tele-surgery. He currently serves as teacher in the Argentine Acupuncture Society, as Invited Foreigner Professor at the China National Academy of Sciences and Hainan Medical University, and as editorial member and reviewer for many internationally renowned journals. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJCC* as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Yan-Xia Xing; Production Department Director: Yun-Xiaojuan Wu; Editorial Office Director: Jin-Lai Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Semimonthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

October 6, 2020

COPYRIGHT

© 2020 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Retrospective Study

Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients

Lang Wang, Wen-Bo He, Xiao-Mei Yu, Da-Long Hu, Hong Jiang

ORCID number: Lang Wang 0000-0003-0739-1481; Wen-Bo He 0000-0003-4687-5622; Xiao-Mei Yu 0000-0002-2109-497X; Da-Long Hu 0000-0003-2047-2868; Hong Jiang 0000-0003-2895-3295.

Author contributions: Wang L and He WB drafted the manuscript; Jiang H and Wang L conceived the idea; Wang L, He WB and Yu XM reviewed the medical records and collected the data; Hu DL performed the statistical analysis and reviewed the manuscript; Jiang H reviewed the manuscript; All authors have read and approved the final manuscript.

Supported by the National Natural Science Foundation of China, No. 81570450 and No. 81900455.

Institutional review board statement: This study was reviewed and approved by the National Natural Science Foundation of China.

Informed consent statement: The National Natural Science Foundation of China waived the informed consent for this study.

Conflict-of-interest statement: There is no conflict of interests.

Data sharing statement: No additional data are available.

Lang Wang, Wen-Bo He, Xiao-Mei Yu, Hong Jiang, Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan 430060, Hubei Province, China

Lang Wang, Wen-Bo He, Xiao-Mei Yu, Hong Jiang, Cardiovascular Research Institute, Wuhan University, Wuhan 430060, Hubei Province, China

Lang Wang, Wen-Bo He, Xiao-Mei Yu, Hong Jiang, Hubei Key Laboratory of Cardiology, Wuhan 430060, Hubei Province, China

Da-Long Hu, School of Biotechnology and Biomolecular Sciences, The University of New South Wales, Sydney 2052, Australia

Corresponding author: Hong Jiang, MD, Chief Physician, Director, Full Professor, Department of Cardiology, Renmin Hospital of Wuhan University, No. 238 Jiefang Road, District of Wuchang, Wuhan 430060, Hubei Province, China. hong-jiang@whu.edu.cn

Abstract

BACKGROUND

The prognostic value of coagulation disorder in coronavirus disease 2019 (COVID-19) patients should be demonstrated.

AIM

To investigate the abnormalities of coagulation parameters in the patients with COVID-19 and their prognostic values.

METHODS

Consecutive patients admitted in the isolation ward of Renmin Hospital of Wuhan University from January 31 to February 5, 2020 with confirmed COVID-19 were included. The primary outcomes were death and survival as of March 11. Demographics, vital signs, comorbidities and laboratory tests were collected and compared between those who died and survivors. Logistic regression analysis for prognostic factors was performed. Kaplan-Meier analysis was used to compare the estimated survival rate between patients with prolonged prothrombin time and normal prothrombin time.

RESULTS

The total number of patients with confirmed COVID-19 who were enrolled was 213. The median age was 62 years, and 95 patients (44.6%) were men. Fifty-one

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Received: April 28, 2020

Peer-review started: April 28, 2020

First decision: May 21, 2020

Revised: June 2, 2020

Accepted: September 8, 2020

Article in press: September 8, 2020

Published online: October 6, 2020

P-Reviewer: Pedrazzani C, Sung WW, Zhang J

S-Editor: Zhang H

L-Editor: Filipodia

P-Editor: Wang LL



patients were critical (23.9%), 79 patients were severe (37.1%) and 83 patients were moderate (39%). As of March 11, 2020, 99 patients were discharged (46.5%), 79 patients (37.1%) stayed in the hospital and 35 patients (16.2%) died. Median time to death was 6 (4-8) d, while median hospital stay was 32 (22-36) d in survivors ($P < 0.001$). More men ($P = 0.002$) and elderly patients ($P < 0.001$) were found in the group of those who died. The respiration rate at admission was higher in the group of those who died ($P < 0.001$). The incidences of hypertension ($P = 0.028$), cerebrovascular disease ($P < 0.001$), chronic kidney disease ($P = 0.02$) and chronic obstructive pulmonary disease ($P < 0.001$) were higher in the group of those who died. Platelet count was decreased in the group of those who died ($P = 0.002$) whereas prothrombin time ($P < 0.001$), activated partial thromboplastin time ($P = 0.033$), concentration of D-dimer ($P < 0.001$) and fibrin degradation products ($P < 0.001$) were increased in the group of those who died. Prothrombin time [odds ratio (OR): 2.19, $P = 0.004$], respiration rate (OR: 1.223, $P < 0.001$), age (OR: 1.074, $P < 0.001$) and fibrin degradation products concentration (OR: 1.02, $P = 0.014$) were predictors of death. The survival rate was significantly lower in patients with prolonged prothrombin time compare to those with normal prothrombin time ($P < 0.001$).

CONCLUSION

Prothrombin time, concentration of fibrin degradation products, respiration rate and age were predictive factors for clinical outcomes of COVID-19 patients.

Key Words: COVID-19; Coagulation; Prothrombin time; Fibrin degradation products; Prognosis; Infectious disease

©The Author(s) 2020. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Coagulation disorders were significantly more common in the patients who died with coronavirus disease 2019 than the survivors. Prothrombin time (PT), concentration of fibrin degradation products, respiration rate and age were predictive factors for fatal outcome. The fatality of patients with prolonged PT at admission was significantly higher than those with normal PT. Patients with prolonged PT at admission should be paid more attention to and treated with caution.

Citation: Wang L, He WB, Yu XM, Hu DL, Jiang H. Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients. *World J Clin Cases* 2020; 8(19): 4370-4379

URL: <https://www.wjgnet.com/2307-8960/full/v8/i19/4370.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v8.i19.4370>

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Since the first COVID-19 case was diagnosed in December 2019, the SARS-CoV-2 has been spreading rapidly around the world. As of March 19, it has caused 209839 infection cases including 8778 deaths^[1]. According to the preliminary statistics from the Chinese Center for Disease Control and Prevention, nearly 20% of the patients were severe to critical, and the case-fatality rate of which was much higher than the whole patient population^[2]. The disease progressed extremely fast in some severe to critical patients. Thus, early identification of COVID-19 patients at high risk is important for improving the clinical practice and outcomes.

Coagulation disorder has been reported in COVID-19 patients in several descriptive studies^[3-5]. The elevation of D-dimer and fibrin degradation products (FDP), shortened or prolonged prothrombin time (PT), abnormal platelet count, occurrence of thrombosis or bleeding and complication of disseminated intravascular coagulation (DIC) were observed in COVID-19 patients in different clinical stages^[6,7]. These findings indicate that the coagulation disorder played an important role in the clinical process of COVID-19. Coagulation disorder at the end-stage of COVID-19 or after invasive treatment is common and reasonable but with limited prognostic value. The

coagulation function at the early stage of hospitalization should be paid more attention to, which may help the doctors to identify patients at high risk and guide the clinical strategy.

MATERIALS AND METHODS

Study design and participants

This is a retrospective, single-center study. Confirmed COVID-19 cases admitted from January 31 to February 5, 2020 to Renmin Hospital of Wuhan University were enrolled in this study. The patients with recent trauma, anticoagulation treatment, confirmed thrombosis or bleeding before hospitalization were excluded. The diagnosis of COVID-19 was based on the interim guidance for novel coronavirus pneumonia published by the National Health Commission of the People's Republic of China^[8]. Patients with COVID-19 were divided into mild, moderate and severe according to the report of the World Health Organization-China joint mission on COVID-19^[9]. Laboratory confirmed cases without pneumonia were classified as mild, laboratory confirmed cases with pneumonia were classified as moderate, patients with dyspnea, respiratory frequency ≥ 30 /min, blood oxygen saturation $\leq 93\%$, $\text{PaO}_2/\text{FiO}_2$ ratio < 300 , and/or lung infiltrates in $> 50\%$ of the lung field within 24-48 h were classified as severe. The patients with respiratory failure requiring mechanical ventilation, shock or other organ failure that required intensive care were classified as critical. This study (WDRY2020-K032) was approved by the Ethics Committee of Renmin Hospital of Wuhan University.

Procedures

Specific nucleic acid of SARS-CoV-2 was detected using real-time polymerase chain reaction to confirm viral infection. Chest X-ray and/or computed tomography were performed for the COVID-19 diagnosis. The patients' medical records were reviewed by trained physicians. Demographics, vital signs, comorbidities, laboratory results of platelet count and coagulation function were collected. All the vital signs were achieved at admission. Comorbidities including hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD), malignancy and autoimmune diseases were collected from patient history. All the blood samples for laboratory tests were collected within 24 h after admission. Platelet count was determined using the Sysmex XN-9000 (Japan), an automated hematology analyzer. The PT, activated partial thromboplastin time (APTT) and thrombin time (TT) were determined by the clot formation technique. The concentration of fibrin, FDP and D-dimer were quantified by the nephelometric analysis. All the coagulation tests were performed using a Sysmex CS5100 automatic coagulation analyzer (Japan) and proprietary reagents. The normal ranges of the laboratory findings were according to the test manual and reagent description of Renmin Hospital of Wuhan University.

Statistical analysis

Basic statistical analyses were performed using Statistic Package for Social Science version 26.0 (Chicago, IL, United States). The normality of continuous variables was tested using the Kolmogorov-Smirnov test. Hypothesis testing was performed for comparing continuous and categorical variables in different outcome groups using the Mann-Whitney *U* test and chi-squared test, respectively. The comorbidities, clinical and laboratory variables that differed significantly based on comparative statistics were included in univariate and multivariate analysis. Variables with statistical significance in the univariate logistic regression were included in the multivariate analysis using forward stepwise logistic regression. The survival rates were analyzed using Kaplan-Meier analysis. All significance levels were computed for two-tailed testing and the cutoff of significance was set at $P < 0.05$ and high significance at $P < 0.001$.

RESULTS

Outcomes

The clinical outcomes were survival and death as of March 11, *i.e.* 5 wk after the last admission. According to the interim guidance for novel coronavirus pneumonia

published by the National Health Commission of the People's Republic of China^[8], patients were discharged when their symptoms improved significantly, with no fever for at least 3 d, obvious absorption of inflammation on pulmonary imaging and negative results for at least two consecutive SARS-CoV-2 nucleic acid tests with an interval of more than 24 h. Patients who did not meet the discharge standard stayed at the hospital for treatment. The discharged patients and those who stayed in the hospital until the end date of follow-up were grouped in the survival group.

Demographics and baseline clinical characteristics

Of 213 patients enrolled, the median age was 62 years, and 95 were men (44.6%). As presented in [Table 1](#), 61% of the enrolled patients were classified as severe or critical. All the patients who died were critically ill. By Mar 11, 2020, 99 patients were discharged (46.5%), 79 patients (37.1%) stayed in the hospital and 35 patients (16.2%) died. There were more males and elderly patients in the group of those who died. Compared with the survivors, comorbidities including hypertension, cerebrovascular disease, chronic kidney disease and COPD were more prevalent in the group of those who died. Vital signs at admission including heart rate, systolic blood pressure, diastolic blood pressure and respiration rate were compared between groups. The respiration rate was significantly higher in those who died.

The onset-to-admission time was compared between the survivors and those who died, and no significant difference was found. The length of hospital stay was also analyzed. For the patients who continued hospitalization until the end date of follow-up, the length of stay was defined as the duration from admission to the end date of follow-up. The length of hospital stay in survivors was 32 (22-36) d, while the admission-to-death time was only 6 (4-8) d for those who died.

Laboratory findings

Platelet count and coagulation parameters were analyzed in the present study. Of the included 213 patients, thrombocytopenia was found in 26 (12.2%), and thrombocytosis was found in 10 (4.7%). PT was prolonged in 39 patients (18.8%). Activated APTT was shortened in 27 patients (12.7%) and was prolonged in 56 patients (26.3%). Eight patients (3.8%) were found with prolonged TT. The shortening of PT or TT was not observed in the present study. The fibrinogen levels in 9 patients (4.7%) were below the normal range and were elevated in 105 patients (49.3%). The concentrations of D-dimer were increased in 123 patients (57.7%), and the concentrations of FDP were elevated in 66 patients (31%).

Comparison of platelet count, coagulation function parameters and the incidence of abnormalities in coagulation indices between survivors and those who died are shown in [Table 2](#). The platelet count was significantly lower in those who died, whereas PT, APTT and the concentrations of D-dimer and FDP were all significantly higher in those who died. There were significant differences in the incidences of thrombocytopenia, PT prolongation, APTT prolongation, TT prolongation, fibrinogen reduction, D-dimer elevation and FDP elevation between those who survived and those who died.

Univariate and multivariate analysis for the prognostic factors

Univariate and multivariate logistic regressions were used to analyze the risk factors for fatal outcome ([Table 3](#)). The factors with significant differences between the death and survival groups, including age, sex, comorbidities, respiration rate, platelet count, PT, APTT, D-dimer and FDP, were included in the regression. Univariate analysis showed that age, sex, hypertension, cerebrovascular disease, chronic kidney disease, COPD, respiration rate, PT, concentrations of D-dimer and FDP may contribute to the death risk of COVID-19 patients. Then those factors with statistical significance in the univariate regression were taken for the multivariate analysis using forward stepwise logistic regression, in which PT [odds ratio (OR): 2.19, 95% confidence interval (CI): 1.285-3.733, $P = 0.004$], respiration rate (OR: 1.223, 95%CI: 1.095-1.366, $P = 0.001$), age (OR: 1.074, 95%CI: 1.034-1.115, $P = 0.001$) and FDP concentration (OR: 1.02, 95%CI: 1.004-1.037, $P = 0.014$) remained to be the significant predictors for death in the multivariate logistic model.

Survival curves in patients with prolonged PT and normal PT

The survival curves of patients with prolonged PT and normal PT were plotted, and the survival rates were analyzed using Kaplan-Meier analysis ([Figure 1](#)). The survival rate at day 5 of hospitalization in normal PT group and prolonged PT group were estimated at 95.8% \pm 1.6% and 76.9% \pm 6.7%, respectively. The survival rate at day 11

Table 1 Baseline characteristics of patients enrolled

Characteristics	Total, n = 213	Survival, n = 178	Death, n = 35	P value, death vs survival
Age in yr, median (IQR)	62 (51-69)	60 (49-67)	73 (65-84)	< 0.001
Sex				
Male	95 (44.6%)	71 (39.9%)	24 (68.6%)	0.002
Comorbidities				
Hypertension	59 (27.7%)	44 (24.7%)	15 (42.8%)	0.028
Diabetes	22 (10.3%)	18 (10.1%)	4 (11.4%)	0.815
Cardiovascular disease	17 (8.0%)	12 (6.7%)	5 (14.3%)	0.132
Cerebrovascular disease	10 (4.7%)	4 (2.2%)	6 (17.1%)	< 0.001
Chronic kidney disease	9 (4.2%)	5 (2.8%)	4 (11.4%)	0.02
COPD	10 (4.7%)	4 (2.2%)	6 (17.1%)	< 0.001
Malignancy	10 (4.7%)	8 (4.5%)	2 (5.7%)	0.755
Autoimmune disease	4 (1.9%)	3 (1.7%)	1 (2.9%)	0.641
Vital signs at admission				
Heart rate as bpm, median (IQR)	85 (78-92)	84 (76-91)	86 (79-95)	0.198
SBP in mmHg, median (IQR)	125 (116-135)	125 (118-134)	124 (110-143)	0.535
DBP in mmHg, median (IQR)	76 (70-80)	77 (70-80)	74 (65-86)	0.683
Respiration rate times per min, median (IQR)	20 (18-21)	19 (18-20)	23 (19-27)	< 0.001
Spectrum				
Moderate	83 (39.0%)	83 (46.6%)	0	
Severe	79 (37.1%)	79 (44.4%)	0	
Critical	51 (23.9%)	16 (9.0%)	35 (100.0%)	
Symptom onset to admission/d, median (IQR)	10 (7-12)	10 (7-12)	10 (7-14)	0.453
Hospitalization stay in d, median (IQR)	27 (14-35)	32 (22-36)	6 (4-8)	< 0.001

BPM: Beats per min; COPD: Chronic obstructive pulmonary disease; DBP: Diastolic blood pressure; IQR: Interquartile range; SBP: Systolic blood pressure.

in normal PT group and prolonged PT group were estimated at $90.4\% \pm 2.3\%$ and $64.1\% \pm 7.7\%$, respectively. According to the result of Log-rank, Breslow and Tarone-Ware tests, the survival curves of the two groups have a highly significant difference ($P = 0.001$).

DISCUSSION

In the present study, we investigated the prognostic value of coagulation parameters in patients with COVID-19 based on at least 5 wk of follow-up. Prolonged PT at admission was found to be a strong predictor for a poor outcome in COVID-19 patients as well as age, respiration rate and FDP concentration, which were also found to contribute to the risk of death in COVID-19 patients.

Renmin Hospital of Wuhan University is a designated hospital for severe COVID-19 patients. In the present study, 35 of 213 patients had died by the 5 wk follow-up, and the CRF was 16.4%, which was higher than the whole patient population. Up to 61% of the enrolled patients were severe to critical, which might contribute to the higher fatality rate. The median survival time for those who died was 6 d, indicating that the disease progressed rapidly in some critical patients. Elderly age and more males were more commonly found in the group of those who died, which was consistent with previous reports^[2]. Comorbidities including hypertension, cerebrovascular disease, chronic kidney disease and COPD, which are more common in the elderly people, were more prevalent in the group of those who died in the present study. The median

Table 2 Laboratory findings at admission

	Normal Range	Total, n = 213	Survival, n = 178	Death, n = 35	P value, death vs survival
Platelet count × 10 ⁹ /L, median (IQR)	125-350	204 (152-255)	211 (157-264)	169 (117-208)	0.002
Blood coagulation					
PT/s, median (IQR)	9-13	12.1 (11.5-12.7)	12 (11.5-12.6)	12.9 (12.0-14.0)	< 0.001
APTT/s, median (IQR)	25-31.3	28.8 (26.5-31.3)	28.6 (26.2-31.2)	29.8 (28.2-32.9)	0.033
TT/s, median (IQR)	14-21	17.3 (16.5-18.3)	17.3 (16.4-18.2)	17.6 (16.7-19.5)	0.099
Fibrinogen in g/L, median (IQR)	2-4	4.10 (3.32-5.12)	4.17 (3.39-5.12)	3.94 (2.49-5.18)	0.294
D-dimer in mg/L, median (IQR)	0-0.55	0.73 (0.40-1.95)	0.62 (0.37-1.63)	2.72 (0.91-17.45)	< 0.001
FDP in mg/L, median (IQR)	0-5	2.72 (1.05-7.05)	2.10 (0.98-5.33)	9.68 (3.20-90.68)	< 0.001
Incidence of coagulation abnormalities					
Thrombocytopenia		26 (12.2%)	17 (9.6%)	9 (25.7%)	0.02
Thrombocytosis		10 (4.7%)	10 (5.6%)	0	0.374
PT prolongation		39 (18.8%)	23 (14.6%)	16 (45.7%)	< 0.001
APTT prolongation		56 (26.3%)	41 (23.0%)	15 (42.6)	0.02
APTT shortening		27 (12.7%)	25 (14.0%)	2 (5.7%)	0.265
TT prolongation		8 (3.8%)	3 (1.7%)	5 (14.2%)	0.004
Fibrinogen elevation		105 (49.29%)	89 (50%)	16 (45.7%)	0.708
Fibrinogen reduction		9 (4.7%)	5 (2.8%)	4 (11.4%)	0.043
D-dimer elevation		123 (57.7%)	92 (51.7%)	31 (88.6%)	< 0.001
FDP elevation		66 (31.0%)	47 (26.4%)	19 (54.3%)	0.002

APTT: Activated partial thromboplastin time; COPD: Chronic obstructive pulmonary disease; FDP: Fibrin degradation products; IQR: Interquartile range; PT: Prothrombin time; TT: Thrombin time.

heart rate and blood pressure at admission were all in the normal range both in survivors and those who died, indicating the vital signs of most patients were stable at admission. The respiration rate was significantly higher in those who died. The increased respiration rate might reflect the severity of lung lesions and hypoxic conditions in COVID-19 patients.

Coagulation disorder has been reported in various viral infections including SARS-CoV, MERS-CoV and influenza virus infection^[10-14]. All aspects of the coagulation cascade, primary hemostasis and fibrinolysis could be affected. The coagulation parameters not only reflect the hemostasis but also associate with the inflammation and organ dysfunction^[15]. In the present study, the comparison of laboratory findings between those who died and survivors showed a significant difference in platelet count and coagulation parameters. Both thrombocytopenia and thrombocytosis were found in COVID-19 patients. However, platelet count in those who died was significantly lower than that in the survivors. The incidence of thrombocytopenia was correspondingly higher in those who died. Similar findings in platelet count had been reported in SARS-CoV infection^[16]. Consumption associated with thrombin-mediated platelet activation and adhesion to endothelial cells and leucocytes could contribute to the reduction of circulating platelets in the critically ill patients^[17].

No patients showed shortened PT, whereas prolonged PT was found in 18.8% of the patients in the present study. The PT and APTT were significantly longer in those who died, but there was no difference with TT. The incidences of PT and APTT prolongation were also increased in those who died. PT and APTT evaluate the integrity of the extrinsic and intrinsic pathways of coagulation, respectively, while both PT and APTT are affected by the final common pathway^[18,19]. The prolonged PT and APTT in those who died might indicate the activation of coagulation and the consumption of coagulation factors.

Elevation of D-dimer and FDP were found in 57.7% and 31% of the COVID-19

Table 3 Univariate and multivariate logistic regression for prognosis factors

Factors	OR	95%CI	P value
Univariate analysis			
Age	1.083	1.048-1.120	< 0.001
Male	3.288	1.516-7.131	0.003
Hypertension	2.284	2.284-1.078	0.031
Cerebrovascular disease	9.000	2.393-33.854	0.001
Chronic kidney disease	4.465	1.135-17.556	0.032
COPD	9.000	2.393-33.854	0.001
Respiration rate	1.192	1.098-1.293	< 0.001
PT	2.734	1.778-4.202	< 0.001
D-dimer	1.062	1.021-1.105	0.003
FDP	1.031	1.017-1.044	< 0.001
Multivariate analysis			
Age	1.074	1.034-1.115	< 0.001
RR	1.223	1.095-1.366	< 0.001
PT	2.190	1.285-3.733	0.004
FDP	1.020	1.004-1.037	0.014

CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; FDP: Fibrin degradation products; OR: Odds ratio; PT: Prothrombin time.

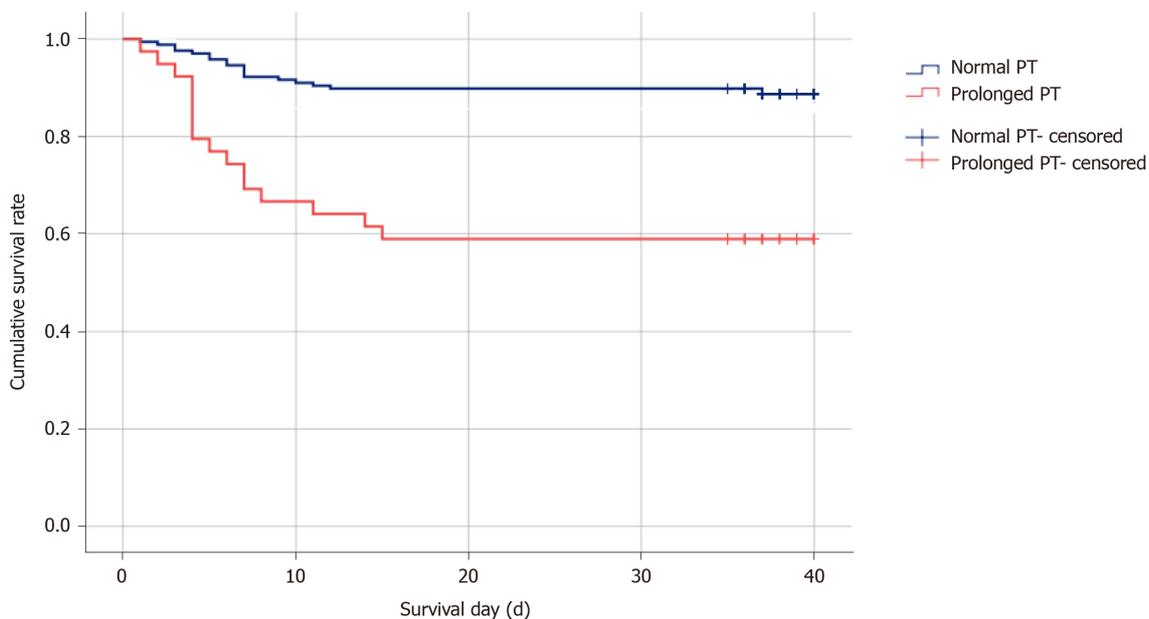


Figure 1 Survival curves of patients with prolonged prothrombin time and normal prothrombin time. The survival curves of patients with prolonged prothrombin time and normal prothrombin time were analyzed using Kaplan-Meier analysis. Log-rank, Breslow and Tarone-Ware tests showed the survival curves of the two groups had a highly significant difference ($P < 0.001$). PT: Prothrombin time.

patients, respectively, which was consistent with previous reports^[3,6]. The median concentrations of D-dimer and FDP were significantly increased in those who died compared with survivors. D-dimer and FDP both originate from the degradation of fibrin and are manifestations for thrombosis and the activation of the fibrinolysis system. Elevation of D-dimer was also associated with severe infection^[15,20]. The raised

D-dimer and FDP concentrations implicate thrombophilia and system inflammation in those COVID-19 patients.

As the platelet count and several parameters of coagulation were significantly different between those who died and survivors, the prognostic value of these factors for COVID-19 was analyzed using logistic regression. PT, concentrations of D-dimer and FDP, age and respiration rate were found to contribute to the fatal outcome in COVID-19 patients. Multivariate analysis showed that PT was a strong prognostic factor with an odds ratio of 2.190 in the COVID-19 patients. FDP concentration was also predictive for the clinical outcomes of COVID-19 patients; however, the prognostic value was limited as the odds ratio was around 1. Age and respiration rate were also found to be prognostic factors in the multivariate analysis, which probably reflect the baseline state and the degree of hypoxia. To further illustrate the impact of PT prolongation on the fatality, the patients were divided into prolonged PT group and normal PT group. Then the survival curve was plotted and analyzed using Kaplan-Meier analysis. The prolonged PT group showed significantly lower estimated survival rate at day 5 of hospitalization, at day 11 of hospitalization and at the end date of follow-up. These data demonstrated that prolonged PT at admission could be a warning sign for high risk of death in the COVID-19 patients.

Tang *et al*^[21] reported the abnormal coagulation in COVID-19 patients. In their study, the comparison of coagulation parameters in survivors and those who died was based on a 10-d to 12-d observation. Significant anomalies of coagulation parameters were observed in those who died, and the development of DIC was more frequent in those who died. DIC is a serious abnormality of coagulation function that usually occurs at the late stage of infectious diseases. In our present study, there were only two patients with DIC (≥ 5 points)^[22] at admission (data not shown). The occurrence of DIC reflects the severity of disease. However, it may not have great predictive value.

In our present study, coagulation parameters at admission were analyzed using multivariate logistic regression, which showed PT is a strong prognosis factors of COVID-19. The PT is a measure of the integrity of the extrinsic and final common pathways of the coagulation cascade that consists of tissue factor and factors VII, II, V, X and fibrinogen. The elevation of PT/international normalized ratio in infectious disease is usually accompanied with low factor levels of VII, IX and X. This is associated with bleeding risk and relates to thrombosis in the patients with infectious disease^[23]. PT could be a relatively early and sensitive indicator for systematic coagulation dysfunction in infectious disease. Our study underscores the need for early detection of coagulation function, which is especially important for risk assessment in COVID-19 patients.

CONCLUSION

Coagulation disorders were significantly more common in the patients who died with COVID-19 than the survivors. Prothrombin time, concentration of fibrin degradation products, respiration rate and age were predictive factors for clinical outcomes of COVID-19 patients. Patients with prolonged prothrombin time at admission should be treated with caution as they were faced with much higher risk of death.

ARTICLE HIGHLIGHTS

Research background

Coronavirus disease 2019 (COVID-19) has been spreading rapidly around the world. The disease progressed extremely fast in some severe to critical patients.

Research motivation

Early identification of COVID-19 patients at high risk is important for improving the clinical practice and outcomes.

Research objectives

To investigate the abnormalities of coagulation parameters in the patients with COVID-19 and their prognostic values.

Research methods

A retrospective, single-center study included 213 patients. The coagulation parameters at admission were compared between the survivors and those who died. The prognostic values of coagulation disorders were analyzed with logistic regression.

Research results

Coagulation disorders were significantly more common in the patients who died with COVID-19 than the survivors. Prothrombin time (PT), concentration of fibrin degradation products, respiration rate and age were predictive factors for fatal outcomes. The fatality of patients with prolonged PT at admission was significantly higher than those with normal PT.

Research conclusions

Patients with prolonged PT at admission were faced with a much higher risk of death. Thus, clinicians should be aware of this and treat these patients with caution.

Research perspectives

Patients with prolonged prothrombin time at admission should be treated with caution as they faced a much higher risk of death. Coagulation disorders were significantly more common in the patients who died with COVID-19.

REFERENCES

- 1 **World Health Organization.** Coronavirus disease 2019 (COVID-19): Situation Report - 59. 2020. Accessed 19 March 2020. Available from: https://www.who.int/docs/default-source/coronavirus/situation-reports/20200319-sitrep-59-covid-19.pdf?sfvrsn=c3dcdcf9_2
- 2 **Epidemiology Working Group for NCIP Epidemic Response;** Chinese Center for Disease Control and Prevention. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020; **41**: 145-151 [PMID: 32064853 DOI: 10.3760/cma.j.issn.0254-6450.2020.02.003]
- 3 **Wang D,** Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020 [PMID: 32031570 DOI: 10.1001/jama.2020.1585]
- 4 **Chen N,** Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395**: 507-513 [PMID: 32007143 DOI: 10.1016/S0140-6736(20)30211-7]
- 5 **Han H,** Yang L, Liu R, Liu F, Wu KL, Li J, Liu XH, Zhu CL. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clin Chem Lab Med* 2020; **58**: 1116-1120 [PMID: 32172226 DOI: 10.1515/cclm-2020-0188]
- 6 **Tao J,** Song Z, Yang L, Huang C, Feng A, Man X. Emergency management for preventing and controlling nosocomial infection of 2019 novel coronavirus: implications for the dermatology department. *Br J Dermatol* 2020; **182**: 1477-1478 [PMID: 321410582020 DOI: 10.1111/bjd.19011]
- 7 **Guan WJ,** Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020; **382**: 1708-1720 [PMID: 32109013 DOI: 10.1056/NEJMoa2002032]
- 8 **National Health Commission of the People's Republic of China.** Interim guidance for novel coronavirus pneumonia (Trial Implementation of Sixth Edition). 2020. Accessed 27 February 2020. Available from: <http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2.shtml>
- 9 **Sung SA,** Jo SK, Cho WY, Won NH, Kim HK. Reduction of renal fibrosis as a result of liposome encapsulated clodronate induced macrophage depletion after unilateral ureteral obstruction in rats. *Nephron Exp Nephrol* 2007; **105**: e1-e9 [PMID: 17106213 DOI: 10.1159/000096859]
- 10 **Singh SK.** Middle East Respiratory Syndrome Virus Pathogenesis. *Semin Respir Crit Care Med* 2016; **37**: 572-577 [PMID: 27486737 DOI: 10.1055/s-0036-1584796]
- 11 **Zumla A,** Hui DS, Perlman S. Middle East respiratory syndrome. *Lancet* 2015; **386**: 995-1007 [PMID: 26049252 DOI: 10.1016/S0140-6736(15)60454-8]
- 12 **Gralinski LE,** Bankhead A 3rd, Jeng S, Menachery VD, Proll S, Belisle SE, Matzke M, Webb-Robertson BJ, Luna ML, Shukla AK, Ferris MT, Bolles M, Chang J, Aicher L, Waters KM, Smith RD, Metz TO, Law GL, Katze MG, McWeeney S, Baric RS. Mechanisms of severe acute respiratory syndrome coronavirus-induced acute lung injury. *mBio* 2013; **4** [PMID: 23919993 DOI: 10.1128/mBio.00271-13]
- 13 **Goeijenbier M,** van Gorp EC, Van den Brand JM, Stittelaar K, Bakhtiari K, Roelofs JJ, van Amerongen G, Kuiken T, Martina BE, Meijers JC, Osterhaus AD. Activation of coagulation and tissue fibrin deposition in experimental influenza in ferrets. *BMC Microbiol* 2014; **14**: 134 [PMID: 24884666 DOI: 10.1186/1471-2180-14-134]
- 14 **Goeijenbier M,** van Wissen M, van de Weg C, Jong E, Gerdes VE, Meijers JC, Brandjes DP, van Gorp EC. Review: Viral infections and mechanisms of thrombosis and bleeding. *J Med Virol* 2012; **84**: 1680-1696 [PMID: 22930518 DOI: 10.1002/jmv.23354]

- 15 **Levi M**, van der Poll T. Coagulation and sepsis. *Thromb Res* 2017; **149**: 38-44 [PMID: 27886531 DOI: [10.1016/j.thromres.2016.11.007](https://doi.org/10.1016/j.thromres.2016.11.007)]
- 16 **Wong RS**, Wu A, To KF, Lee N, Lam CW, Wong CK, Chan PK, Ng MH, Yu LM, Hui DS, Tam JS, Cheng G, Sung JJ. Haematological manifestations in patients with severe acute respiratory syndrome: retrospective analysis. *BMJ* 2003; **326**: 1358-1362 [PMID: 12816821 DOI: [10.1136/bmj.326.7403.1358](https://doi.org/10.1136/bmj.326.7403.1358)]
- 17 **Thachil J**, Warkentin TE. How do we approach thrombocytopenia in critically ill patients? *Br J Haematol* 2017; **177**: 27-38 [PMID: 27982413 DOI: [10.1111/bjh.14482](https://doi.org/10.1111/bjh.14482)]
- 18 **Chee YL**. Coagulation. *J R Coll Physicians Edinb* 2014; **44**: 42-45 [PMID: 24995447 DOI: [10.4997/JRCPE.2014.110](https://doi.org/10.4997/JRCPE.2014.110)]
- 19 **Yang R**, Moosavi L. Prothrombin Time. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 [PMID: 31334989]
- 20 **Fan SL**, Miller NS, Lee J, Remick DG. Diagnosing sepsis - The role of laboratory medicine. *Clin Chim Acta* 2016; **460**: 203-210 [PMID: 27387712 DOI: [10.1016/j.cca.2016.07.002](https://doi.org/10.1016/j.cca.2016.07.002)]
- 21 **Tang N**, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020; **18**: 844-847 [PMID: 32073213 DOI: [10.1111/jth.14768](https://doi.org/10.1111/jth.14768)]
- 22 **Taylor FB Jr**, Toh CH, Hoots WK, Wada H, Levi M; Scientific Subcommittee on Disseminated Intravascular Coagulation (DIC) of the International Society on Thrombosis and Haemostasis (ISTH). Towards definition, clinical and laboratory criteria, and a scoring system for disseminated intravascular coagulation. *Thromb Haemost* 2001; **86**: 1327-1330 [PMID: 11816725 DOI: [10.1055/s-0037-1616068](https://doi.org/10.1055/s-0037-1616068)]
- 23 **Walborn A**, Williams M, Fareed J, Hoppensteadt D. International Normalized Ratio Relevance to the Observed Coagulation Abnormalities in Warfarin Treatment and Disseminated Intravascular Coagulation. *Clin Appl Thromb Hemost* 2018; **24**: 1033-1041 [PMID: 29848060 DOI: [10.1177/1076029618772353](https://doi.org/10.1177/1076029618772353)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

