Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Comparison of Outcomes in Patients With COVID-19 and Thrombosis Versus Those Without Thrombosis

Brian C. Case, MDa, Jonathan Abramowitz, MSa, Corey Shea, MSa, Hank Rappaport, MDa, Giorgio A. Medranda, MDa, Charan Yerasi, MDa, Brian J. Forrestal, MBBSa, Chava Chezar-Azerrad, MDa, Cheng Zhang, PhDa, Lowell F. Satler, MDa, Itsik Ben-Dor, MDa, Hayder Hashim, MDa, Toby Rogers, MD, PhDab, William S. Weintraub, MDa, and Ron Waksman, MDa,*

The occurrence of venous thromboembolisms in patients with COVID-19 has been established. We sought to evaluate the clinical impact of thrombosis in patients with COVID-19 over the span of the pandemic to date. We analyzed patients with COVID-19 with a diagnosis of thrombosis who presented to the MedStar Health system (11 hospitals in Washington, District of Columbia, and Maryland) during the pandemic (March 1, 2020, to March 31, 2021). We compared the clinical course and outcomes based on the presence or absence of thrombosis and then, specifically, the presence of cardiac thrombosis. The cohort included 11,537 patients who were admitted for COVID-19. Of these patients, 1,248 had noncardiac thrombotic events and 1,009 had cardiac thrombosis (myocardial infarction) during their hospital admission. Of the noncardiac thrombotic events, 562 (45.0%) were pulmonary embolisms, 480 (38.5%) were deep venous thromboembolisms, and 347 (27.8%) were strokes. In the thrombosis arm, the mean age of the cohort was 64.5 ± 15.3 years, 53.3% were men, and the majority were African-American (64.9%). Patients with thrombosis tended to be older with more co-morbidities. The in-hospital mortality rate was significantly higher (16.0%) in patients with COVID-19 with concomitant noncardiac thrombosis than in those without thrombosis (7.9%, p <0.001) but lower than in patients with COVID-19 with cardiac thrombosis (24.7%, p <0.001). In conclusion, patients with COVID-19 with thrombosis, especially cardiac thrombosis, are at higher risk for in-hospital mortality. However, this prognosis is not as grim as for patients with COVID-19 and cardiac thrombosis. Efforts should be focused on early recognition, evaluation, and intensifying antithrombotic management for these patients. © 2021 Published by Elsevier Inc. (Am J Cardiol 2021;160:106–111)

Patients infected with SARS-CoV-2, which causes COVID-19, can develop cardiac damage,1,2 and the overall prevalence is high in hospitalized patients.3 Furthermore, patients with known cardiovascular disease are at an increased risk of developing COVID-19, including a more severe form.4 Given these concerning findings, guidelines reinforced primary percutaneous coronary intervention as the standard of care for ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) in patients with high-risk features.5,6 In addition, the direct effects of the virus and the indirect effects of the infection predispose these patients to thrombotic events. A combination of the disseminated intravascular coagulation and the severe inflammatory response, critical illness, and underlying traditional risk factors may all predispose a patient to thrombotic events.7,8 Furthermore, therapies for treating COVID-19 may have adverse drug-drug interactions with antiplatelet agents and anticoagulants. In the present study, we describe our health care system’s experience with COVID-19 patients with thrombosis (stroke and venous thromboembolism [VTE]) in comparison with patients with COVID-19 without VTE in terms of characteristics and clinical outcomes. In addition, we compared these patients with patients with COVID-19 with cardiac thrombosis (myocardial infarction).

Methods

We analyzed patients with COVID-19 who presented to the MedStar Health system (11 hospitals in Washington, District of Columbia, and Maryland) during the pandemic era. The pandemic era was identified as the period from March 1, 2020, through March 31, 2021. A positive test result for the infection was based on polymerase chain reaction testing and the patient presenting with respiratory symptoms and/or having chest x-ray or computed tomography findings.

Evaluating for a thromboembolism was not standardized and was done at the discretion of the provider. A diagnosis...
was made by an imaging modality, including lower-extremity venous duplex for deep VTE and computed tomography or ventilation or perfusion lung scan for a pulmonary embolism. The presence of d-dimer alone did not qualify as a diagnosis of VTE. For stroke, the diagnosis was made on the basis of clinical symptoms of a stroke and supported by an imaging modality. The final diagnosis and inclusion in our analysis was based on the hospital-stay International Classification of Diseases, Tenth Revision (ICD-10).

For the cardiac thrombosis cohort, patients were identified by the ICD-10 codes for the diagnosis of STEMI or NSTEMI. Next, the measurement of troponin levels was not standardized and was conducted at the discretion of the provider. The troponin value that was recorded is the peak level measured during the hospitalization. In our analysis, we included cardiac troponin I (upper limit of normal of 0.03 ng/ml) or high-sensitivity cardiac troponin (upper limit of normal of 30 ng/ml), which are common troponin markers collected in our health care system that were measured for all patients in this analysis. Investigators identified significant presence of troponin I as an elevation >1 ng/ml or high-sensitivity troponin >30 ng/ml.

The baseline characteristics and co-morbidities were collected for all patients. In this analysis, co-morbidities were identified using the ICD-10 codes. Laboratory data and the use of ventilation were compared between the 2 groups. The primary end point was in-hospital mortality. The study was conducted in accordance with the Declaration of Helsinki and was approved by our institutional review board.

Descriptive statistics such as frequencies, means, and SDs were used to describe the study population. Student t test or analysis of variance was used to compare the mean values of normally distributed data. Cox-regression method was used to evaluate risk factors for the primary outcome. Two-tailed Fisher’s exact test or chi-square test was used to compare categorical variables. The odds ratio for in-hospital mortality and ventilation requirement was estimated from a multivariate logistic regression. Statistical significance was considered to be p < 0.05. All analyses were done in SAS version 9.4 (SAS Institute, Cary, North Carolina). One author (B.C.C.) has full access to all the data in the study and takes full responsibility for its integrity and the data analysis.

Results

This study included 11,537 patients with COVID-19 who were admitted during the pandemic. Of these patients, 1,248 (10.8%) had noncardiac thrombotic events (stroke or VTE) during their hospital admission and 1,009 (8.7%) had cardiac thrombosis (myocardial infarction). Of the noncardiac thrombotic events, 562 (45.0%) were pulmonary embolisms, 480 (38.5%) were deep VTEs, and 347 (27.8%) were strokes. The baseline characteristics are displayed in Table 1. In the non-cardiac thrombosis cohort, the majority of patients were men (53.3%) with a mean age of 64.5 ± 15.3 years. Patients with COVID-19 with non-cardiac thrombosis tended to have a higher rate of co-morbidities than patients with COVID-19 without thrombosis. However, the rate of co-morbidities in the non-cardiac thrombosis cohort was lower than in patients with COVID-19 with cardiac thrombosis, except for those with a history of stroke.

During their hospital admissions, the white blood cell count and concentration of creatinine, C-reactive protein, lactate dehydrogenase, and ferritin were significantly higher in patients with thrombosis than in patients without thrombosis. However, these laboratory values and those of troponin and N-terminal prohormone B-type natriuretic peptide were significantly higher in the cardiac thrombosis arm than in the non-cardiac thrombosis and no-thrombosis cohorts. Laboratory data are displayed in Table 2.

Our primary end point, in-hospital mortality (Figure 1), was significantly higher (16.0%) in patients with COVID-19 with non-cardiac thrombosis than in those without a thrombotic event (7.9%, p < 0.001) but was lower than in patients with COVID-19 with cardiac thrombosis (24.7%, p < 0.001). With regard to our secondary end points, patients

| Table 1 | Baseline characteristics of patients with COVID-19 overall, thrombosis present, cardiac thrombosis only, and those without thrombosis |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Demographics    | Overall          | Non-Cardiac Thrombosis* | Cardiac Thrombosis** | No Thrombosis    |
| Age ± SD (years)| (N = 11,537)     | (N = 1,248)      | (N = 1,009)       | (N = 9,280)      |
| Male            | 48.7%            | 53.3%            | 53.4%            | 47.6%           | 0.001       |
| Ethnicity       |                  |                  |                  |                  |
| White           | 26.3%            | 24.5%            | 26.9%            | 26.5%           | 0.294       |
| Black           | 58.0%            | 64.9%            | 64.5%            | 56.4%           | <0.001      |
| Asian           | 1.3%             | 0.9%             | 1.5%             | 1.4%            | 0.350       |
| Native American | 0.2%             | 0.0%             | 0.1%             | 0.2%            | 0.157       |
| Other           | 14.1%            | 9.7%             | 6.9%             | 15.5%           | <0.001      |
| Co-Morbidities  |                  |                  |                  |                  |
| Active malignancy| 8.0%             | 9.5%             | 9.7%             | 7.6%            | 0.008       |
| Heart disease   | 27.3%            | 33.3%            | 64.3%            | 22.4%           | <0.001      |
| Diabetes mellitus| 33.8%            | 45.5%            | 35.0%            | 32.4%           | <0.001      |
| Kidney disease  | 8.9%             | 9.4%             | 20.2%            | 7.7%            | <0.001      |
| Liver disease   | 4.1%             | 5.3%             | 5.9%             | 3.7%            | <0.001      |
| Lung disease    | 36.7%            | 34.2%            | 47.1%            | 35.9%           | <0.001      |

* Venothromboembolism and Pulmonary Embolism.
* ST-Elevation Myocardial Infarction and Non-ST Elevation Myocardial Infarction.
with COVID-19 with non-cardiac thrombosis required ventilation (28.2%) at a higher rate than patients with COVID-19 with cardiac thrombosis (26.8%) or those without thrombosis (9.7%). Primary and secondary end point data are displayed in Table 3.

Finally, the odds ratio for in-hospital mortality (area under the receiver operator characteristic curve of 0.85) and ventilation requirement (area under the receiver operator characteristic curve of 0.84) was estimated from a multivariate logistic regression and the results are presented in Table 4. Thrombosis versus no thrombosis appeared to be significant for in-hospital mortality, whereas thrombosis versus no thrombosis and then cardiac thrombosis versus noncardiac thrombosis appeared to be significant for ventilation requirement.

Discussion

The primary findings of our analysis suggest that patients with COVID-19 with concomitant non-cardiac thrombosis have a significantly increased risk of mortality when compared with patients with COVID-19 without thrombosis but

Table 2
Laboratory data of patients with COVID-19 overall, thrombosis present, cardiac thrombosis only, and those without thrombosis

| Variable | Overall (N = 11,537) | Non-Cardiac Thrombosis* (N = 1,248) | Cardiac Thrombosis** (N = 1,009) | No Thrombosis (N = 9,280) | p Value |
|----------|----------------------|-------------------------------|---------------------------|----------------------|---------|
| Maximum troponin-I (ng/mL) | 0.59 +/- 6.32 | 0.64 +/- 4.97 | 4.1 +/- 17.42 | 0.09 +/- 1.63 | <0.001 |
| Maximum high-sensitivity troponin (ng/mL) | 310.7 +/- 2824.62 | 784.65 +/- 5604.18 | 1,590.25 +/- 6145.03 | 77.93 +/- 539.01 | <0.001 |
| N-terminal-pro-hormone BNP (ng/L) | 5,321.95 +/- 20,010.59 | 4,754.7 +/- 14,685.15 | 15,151.82 +/- 34,976.65 | 3,630.63 +/- 16,015.69 | <0.001 |
| Maximum creatinine (mg/dL) | 2.08 +/- 2.5 | 2.5 +/- 2.71 | 3.51 +/- 3.62 | 1.88 +/- 2.27 | <0.001 |
| Maximum white blood cell (K/μL) | 8.94 +/- 8.88 | 10.2 +/- 6.62 | 10.17 +/- 8.83 | 8.68 +/- 9.09 | <0.001 |
| C-reactive protein (mg/dL) | 69.89 +/- 54.42 | 78.68 +/- 54.22 | 85.4 +/- 61.5 (394) | 67.04 +/- 53.18 | <0.001 |
| Lactate dehydrogenase (U/L) | 420.73 +/- 299.6 | 420.73 +/- 299.6 | 553.76 +/- 538.32 | 397.74 +/- 247.57 | <0.001 |
| Ferritin (ng/mL) | 1,071.99 +/- 2,409.21 | 1,337.77 +/- 2,456.67 | 1,967.09 +/- 4,165.48 | 1,967.09 +/- 4,165.48 | <0.001 |

BNP = B-type natriuretic peptide.
* Venothromboembolism and Pulmonary Embolism.
* ST-Elevation Myocardial Infarction and Non-ST Elevation Myocardial Infarction.
not as high of a risk as patients with COVID-19 with cardiac thrombosis. Patients with COVID-19 with non-cardiac thrombosis tended to require ventilation at a higher rate than patients with COVID-19 with cardiac thrombosis and those without any thrombosis.

There are multiple factors that contribute to the development of thrombosis in patients with COVID-19. First, patient risk factors include acute critical illness, being bedridden, active infection or sepsis, underlying liver or kidney disease, or the presence of a malignancy. In our analysis, co-morbidities were significantly higher in patients with thrombosis than in patients without thrombosis. Second, the infection itself causes an inflammatory response with lymphopenia, elevated fibrinogen, and increased inflammatory markers and cytokines. Furthermore, SARS-CoV-2 infection leads to further superimposed infections. Again, these findings were demonstrated to be higher in our analysis with increased white blood cell count and concentration of creatinine, C-reactive protein, lactate dehydrogenase, and ferritin in the thrombosis arm. This reiterates the importance of checking for these markers because they may help in predicting outcomes and guiding the treatment.

The combination of patient risk factors and the SARS-CoV-2 infection leads to intravascular coagulopathy, which causes myocardial injury and pulmonary microthrombi. These abnormalities ultimately lead to VTE, myocardial infarction, hyperinflammation, and, in some cases, disseminated intravascular coagulation. Furthermore, there is the concept of “thromboinflammation,” which is thrombosis leading to more inflammatory activation. This phenomenon can be challenging to treat and has been seen in patients with COVID-19. As outlined by our analysis, patients with thrombosis carry a worse prognosis than patients without thrombosis. However, myocardial infarction in patients with COVID-19 carry the worst prognosis.

One way to ensure a favorable outcome is rapid disease awareness and early admission of the patient to the hospital for treatment therapy, especially for anticoagulation and antithrombotic therapy. Throughout the course of the COVID-19 pandemic, treatment strategies evolved significantly as the guidelines changed and clinical knowledge improved. In the early stages of the pandemic, the standard of care was initially supportive, including the use of supplemental oxygen, prone positioning, and conservative fluid management. Prophylactic antibiotics, management of co-morbidities, avoiding mechanical ventilation whenever possible, and a variety of antithrombotic management protocols. More recently, the use of corticosteroids, in particular dexamethasone, is recommended for patients with COVID-19 who require supplemental oxygen or mechanical ventilation to decrease all-cause mortality. Other treatment strategies include convalescent plasma infusions. Finally, in October 2020, the antiviral medication remdesivir received Emergency Use Authorization from the US Food and Drug Administration because it was shown to be superior to a placebo at reducing the time to recovery in those hospitalized patients with COVID-19; however, more recent data on remdesivir may not support this finding as strongly.

Furthermore, the prevention and treatment of thrombosis in patients with COVID-19 has evolved. For patients hospitalized with COVID-19, pharmacologic VTE prophylaxis should be initiated unless contraindicated. In addition, the results from 3 large international clinical trials conducted by the National Institutes of Health suggest that full-dose antiocoagulation therapy improved outcomes for patients hospitalized with moderate COVID-19 (in terms of ventilation need and reduced mortality rate). This may be a treatment strategy for critically ill patients. Parenteral anticoagulation is recommended in most cases in which anticoagulant therapy is needed for known thrombotic disease. Unfractionated heparin can be used in the setting of anticipated procedures or in patients with deteriorating renal function. If no urgent procedures are anticipated, low-molecular-weight heparin is a reasonable alternative.

Finally, our analysis demonstrates that myocardial infarction in patients with COVID-19 is a concern. Early in

---

Table 3
Primary and secondary outcomes. In-hospital mortality and ventilator requirement of patients with COVID-19 during the pandemic era overall, with thrombosis present, cardiac thrombosis only, and those without thrombosis.

| Variable                     | Overall (N = 11,537) | Non-Cardiac Thrombosis* (N = 1,248) | Cardiac Thrombosis** (N = 1,009) | No Thrombosis (N = 9,280) | p Value |
|------------------------------|----------------------|-------------------------------------|--------------------------------|--------------------------|---------|
| Overall In-Hospital Mortality| 10.2%                | 16.0%                               | 24.7%                          | 7.9%                     | <0.001  |
| Ventilator Requirement       | 13.2%                | 28.2%                               | 26.8%                          | 9.7%                     | <0.001  |

* Venothromboembolism and Pulmonary Embolism.
* ST-Elevation Myocardial Infarction and Non-ST Elevation Myocardial Infarction.

---

Table 4
Adjusted in-hospital mortality in patients with COVID-19. Adjusted odds ratios of thrombosis versus no thrombosis and cardiac thrombosis versus non-cardiac thrombosis, adjusting for inflammatory markers.

| In-hospital mortality | Odds Ratio | 95% confidence interval |
|-----------------------|------------|-------------------------|
| Thrombosis versus no thrombosis | 0.68 | 0.50 – 0.93 |
| Cardiac thrombosis versus non-cardiac thrombosis | 1.19 | 0.80 – 1.77 |
| Creatinine           | 1.08 | 1.04 – 1.11 |
| C-reactive protein   | 1.01 | 1.01 – 1.01 |
| Lactate dehydrogenase| 1.00 | 1.00 – 1.00 |
| Ferritin             | 1.00 | 1.00 – 1.00 |

| Ventilation requirement | Odds Ratio | 95% Confidence Interval |
|-------------------------|------------|-------------------------|
| Thrombosis versus no thrombosis | 0.32 | 0.25 – 0.42 |
| Cardiac thrombosis versus non-cardiac thrombosis | 0.63 | 0.44 – 0.89 |
| Creatinine           | 1.10 | 1.07 – 1.14 |
| C-reactive protein   | 1.01 | 1.04 – 1.08 |
| Lactate dehydrogenase| 1.00 | 1.00 – 1.00 |
| Ferritin             | 1.00 | 1.00 – 1.00 |
the pandemic, providers may have been more likely to regard elevated troponins as a marker of obstructive coronary artery disease and recommend an angiography. Later in the pandemic, providers may have been aware of the increasing evidence that troponin elevations are seen in patients with COVID-19 without obstructive coronary artery disease and, thus, chose to forgo invasive testing. Particular attention has been directed toward the management of acute coronary syndrome during the COVID-19 pandemic. In patients with STEMI or NSTEMI with high-risk features in which the etiology of their acute myocardial infarction is suspected to be true plaque rupture and not myocarditis or stress-induced cardiomyopathy in the setting of SARS-CoV-2 infection, our cardiac catheterization laboratory implemented procedures to ensure the safety of medical personnel during primary percutaneous coronary intervention. Per the guidelines recommended by the American College of Cardiology’s Intervention Council and the Society for Cardiovascular Angiography and Interventions, we trained everyone in the catheterization laboratory on proper personal protective equipment use, designated 1 laboratory for patients with COVID-19 or those who were under investigation, and performed extensive cleaning after each procedure. We also implemented new treatment and risk stratification algorithms, utilizing noninvasive diagnostic testing such as echocardiography and cardiac magnetic resonance imaging in patients with low-risk features, to ensure that only high-risk patients with COVID-19 with suspected plaque rupture were brought to the catheterization laboratory.27

There are limitations to our study. First, the analysis is retrospective and relies on the ICD-10 codes to identify the patient population. Inclusion in our analysis depended only on a positive COVID-19 test and a diagnosis of a thrombotic event as reported by the provider. In addition, STEMI or NSTEMI patients’ coronary angiographic findings were not fully captured in our analysis. Analysis of these data would have allowed us to completely separate those with obstructive coronary artery disease from those with other etiologies of myocardial injury (e.g., myocarditis or stress-induced cardiomyopathy).28 Furthermore, although we captured whether patients were diagnosed, we did not capture the treatment strategy (pharmacologic, mechanical, and so on). Finally, our data captured patients in the Mid-Atlantic region of the United States where the pandemic had the greatest impact in March 2020 and April 2020. Our findings may not represent the broader United States outcome data.

In conclusion, our analysis suggests that patients with COVID-19 with non-cardiac thrombosis are at higher risk for in-hospital mortality. However, this prognosis is not as grim as for patients with cardiac thrombosis. Efforts should focus on early recognition, evaluation, and intensifying care of these patients.

Disclosures

Dr. Rogers reports serving as a proctor and consultant for Medtronic and Edwards Lifesciences, serving on the advisory board for Medtronic, and holding equity interest in Transmural Systems. Dr. Waksman reports serving as an advisory board member for Amgen, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, and Pi-Cardia Ltd.; serving as a consultant for Amgen, Biotronik, Boston Scientific, Cardiovascular Systems Inc., Medtronic, Philips, and Pi-Cardia Ltd.; receiving grant support from AstraZeneca, Biotronik, Boson Scientific, and Chieisi; serving on the speakers bureau for AstraZeneca and Chieisi; and being an investor in MedAlliance. The remaining authors have no conflicts of interest to disclose.

Acknowledgment

A special acknowledgment to Jason Wermers, MS, for assistance in preparing this manuscript.

1. Xiong TY, Redwood S, Prendergast B, Chen M. Coronavirus and the cardiovascular system: acute and long-term implications. Eur Heart J 2020;41:1798–1800.
2. Schoenhagen P, Tuzcu EM, Ellis SG. Plaque vulnerability, plaque rupture, and acute coronary syndromes: (multi)-focal manifestation of a systemic disease process. Circulation 2002;106:760–762.
3. Sandoval Y, Januzzi JL Jr, Jaffe AS. Cardiac troponin for assessment of myocardial injury in COVID-19: JACC review topic of the week. J Am Coll Cardiol 2020;76:1244–1258.
4. Case BC, Yerasi C, Forrestal BJ, Shea C, Rappaport H, Medranda GA, Zhang C, Satler LF, Ben-Dor I, Hashim H, Rogers T, Waksman R. Comparison of characteristics and outcomes of patients with acute myocardial infarction with versus without coronavirus-19. Am J Cardiol 2021;144:8–12.
5. O’Gara PT, Kushner FG, Ascheim DD, Jr Casey DE, Chng MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, American College of Cardiology Foundation, American Heart Association Task Force on Practice Guidelines, American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, American Heart Association Task Force on Practice Guidelines, American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv 2013;82:E1–E27.
6. Welt FGP, Shah PB, Aronov HD, Bortnick AE, Henry TD, Sherwood MW, Young MN, Davidson LJ, Kadavath S, Mahmoud E, Kirtane AJ, American College of Cardiology’s Interventional Council, Society for Cardiovascular Angiography and Interventions. Considerations during the coronavirus (COVID-19) pandemic: from the ACC’s interventional council and SCAI. J Am Coll Cardiol 2020;75:2372–2375.
7. Gjesecka A, Borovac JA, Guerreiro RA, Giustozzi M, Parker W, Caldeira D, Chiva-Blanch G. Thrombotic complications in patients with COVID-19: pathophysiological mechanisms, diagnosis, and treatment. Cardiovasc Drugs Ther 2021;35:215–229.
8. Han BE, Chong VCL, Chan SSW, Lim GH, Lim KGE, Tan GB, Zhang C, Satler LF, Ben-Dor I, Hashim H, Rogers T, Waksman R. Comparison of characteristics and outcomes of patients with acute myocardial infarction with versus without coronavirus-19. Am J Cardiol 2021;144:8–12.
9. Chong PY, Chui P, Ling AE, Franks TJ, Tai DY, Leo YS, Kaw GI, Wansaicheong G, Chan KP, Ean Oon LL, Teo ES, Tan KB, Nakajima N, Sata T, Travis WD. Analysis of deaths during the severe acute respiratory syndrome (SARS) epidemic in Singapore: challenges in determining a SARS diagnosis. Arch Pathol Lab Med 2004;128:195–204.
10. Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, Law KL, Tang BS, Hon TY, Chan CS, Chan KH, Ng JS, Zheng BJ, Ng WL, Lai RW, Guan Y, Yuen KY, HKU/UCH SARS Study Group. Clinical progression and viral load in a community outbreak of coronavirus-
associated SARS pneumonia: a prospective study. Lancet 2003;361:1767–1772.
11. Tsui KL, Leung TC, Yam LY, So LK, Poon E, Lung KC, Li SK. Coronary plaque instability in severe acute respiratory syndrome. Int J Cardiol 2005;99:471–472.
12. Umaphati T, Kor AC. Venkatasubramanian N, Lim CC, Pang BC, Yeo TT, Lee CC, Lim PL, Ponnnudurai K, Chua KL, Tan PH, Tai DY. Ang SP. Large artery ischaemic stroke in severe acute respiratory syndrome (SARS). J Neurol 2004;251:1227–1231.
13. Lew TW, Kwok TK, Tai D, Earnest A, Loo S, Singh K, Kwan KM, Umapathi T, Kor AC, Venketasubramanian N, Lim CC, Pang BC, Yeo TT, Lee CC, Lim PL, Ponnnudurai K, Chua KL, Tan PH, Tai DY. Ang SP. Large artery ischaemic stroke in severe acute respiratory syndrome. JAMA 2003;290:374–380.
14. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med 2020;58:1131–1134.
15. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost 2020;18:1421–1424.
16. Mitchell WB. Thromboinflammation in COVID-19 acute lung injury. Paediatr Respir Rev 2020;35:20–24.
17. Boudadma L, Lesercue FX, Lucec JC, Yazdanpanah Y, Timsit JF, Severe SC. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. Intensive Care Med 2020;46:579–582.
18. Coppo A, Bellani G, Winterton D, Di Pierro M, Sorta A, Faverio P, Cairo M, Mori S, Messinesi G, Contro E, Bonfanti P, Benini A, Valsecchi MG, Antolini L, Foti G. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med 2020;8:765–774.
19. Kazory A, Ronco C, McCullough PA. SARS-CoV-2 (COVID-19) and intravascular volume management strategies in the critically ill. Proc (Bayl Univ Med Cent) 2020;33:1–6.
20. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, Angus DC, Annane D, Azevedo LCP, Bévier W, Béjar J, Cavaletti AB, Dequin PF, Du B, Emberson J, Fisher D, Giraudet B, Gordon AC, Granholt A, Green C, Haynes R, Heming N, Higgins JPT, Horby P, Juni P, Landray MJ, Le Gouge A, Leclerc M, Lim WS, Machado FR, McArthur C, Meziani F, Meller MH, Perner A, Petersen MW, Savovic J, Tomazini B, Veiga VC, Webb S, Marshall JC. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. JAMA 2020;324:1330–1341.
21. Müllerthies K. Colorants de maquillage pour céramique concus [Surface coloring for built ceramic]. Rev Fr Prothet Dent 1988(4B): 37–8, 51–32.
22. Simonovich VA, Burgos Pratx LD, Scibona P, Beruto MV, Vallone MG, Vázquez C, Savoy N, Giunta DH, Pérez LG, Sánchez MDL, Gamarnik AV, Ojeda DS, Santoro DM, Camino PJ, Antelo S, Rainero K, Vidiella GP, Miyazaki EA, Cornstein W, Trabedalo OA, Ross FM, Spotti M, Funtowicz G, Scordo WE, Losso MH, Ferniot I, Pardo PE, Rodríguez E, Rucci P, Pasquali J, Fuentes NA, Esperatti M, Speroni GA, Namini EC, Matteuccio A, Michelangelo HG, Follmann D, Lane HC, Belloso WH, PlasmaR Study Group. A randomized trial of convalescent plasma in COVID-19 severe pneumonia. N Engl J Med 2021;384(7):619–629.
23. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Pardes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh MD, Ruiz-Palacios GM, Benfield T, Fäkkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Landgren J, Bahiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Ousini A, Nayak S, Lane HC, ACTT-1 Study Group Members. Remdesivir for the treatment of COVID-19 - final report. N Eng J Med 2020;383:1813–1826.
24. WHO Solidarity Trial Consortium, Pan H, Peto R, Hennao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, Abdool Karim Q, Alejandria MM, Hernández García C, Kinye MP, Malekzadeh R, Murthy S, Reddy KS, Roses Periago M, Abi Hanna P, Adler F, Al-Bader AM, Alhasawi A, Allum E, Alotaibi A, Alvarez-Moreno CA, Appadoo S, Asiri A, Aukrust P, Barratt-Due A, Bellani S, Branca M, Cappel-Porter HBC, Cerrato N, Chow TS, Como N, Eustace J, García PJ, Godbole S, Gotuzzo E, Griskevicius L, Hamra R, Hassan M, Hassany M, Hutton D, Irmsyah A, Jancoriene L, Kirwan J, Kumar S, Lennon P, Lopardo G, Lydon P, Magrini N, Maguire T, Maneyska S, Manuel O, McGinty S, Medina MT, Mesa Rubio ML, Miranda-Montoya MC, Nel J, Nunes EP, Perola M, Portolés A, Rasmin MR, Raza A, Rees H, Reges FPS, Rogers CA, Salami K, Salvadori MI, Sinani N, Sterne JAC, Stevanovikj M, Tacconelli E, Tikkinen KAO, Trelle S, Saeid H, Rottingen JA, Swaminathan S. Repurposed antiviral drugs for COVID-19 - interim WHO solidarity trial results. N Engl J Med 2021;384:497–511.
25. LaVange L, Adam SJ, Currier JS, Higgs ES, Reinke LA, Hughes EA, Read SW. ACTIV Therapeutics-Clinical Working Group. Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): Designing Master Protocols for Evaluation of Candidate COVID-19 Therapeutics. Ann Intern Med 2021;174:1293–1300.
26. Kahn SR, Lim W, Dunn AS, Cushman M, Dentali F, Akl EA, Cook DJ, Balekian AA, Klein RC, Le H, Schulman S, Murad MH. 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): e195S–e226S.
27. Yerasi C, Case BC, Forrestal BJ, Chezar-Azerrad C, Hashim H, Ben-Dor I, Satler LF, Mintz GS, Waksman R. Treatment of ST-segment elevation myocardial infarction During COVID-19 pandemic. Cardiovasc Revasc Med 2020;21:1024–1029.
28. Khalid N, Chan Y, Case BC, Shlomfisz E, Wermers JP, Rogers T, Ben-Dor I, Waksman R. COVID-19 (SARS-CoV-2) and the heart: an ominous association. Cardiovasc Revasc Med 2020;21:946–949.