ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 10, Issue, 10, pp. 41595-41599, October, 2020
https://doi.org/10.37118/ijdr.20074.10.2020

RESEARCH ARTICLE OPEN ACCESS

SARS-CoV-2 AND CARDIOVASCULAR DISEASES: MAJOR CONSIDERATIONS AND SYSTEMATIC REVIEW

Otávio Queiroz Assumpção[1], Vanessa Piovesan Freitas Assumpção[1], Pedro WagnerRamos Júnior[2], Marcos Eduardo dos Santos Dotto[3], Francisco Corrêa de Almeida Moraes[4], Antonio Carlos Broim Pancotti[5], Caio Fraga Barreto de Matos Ferreira[6], Jaquelini Tirapelle Ayub Ribeiro[7], Monique Souza Bandoli Franca[8], Viviane Ferreira Gali[9] and Idiberto José Zotarelli Filho[10,11]

[1]Fundação Hospitalar de Costa Rica Clínica Vitale (ICCOR)/Costa Rica Hospital Foundation- VitaleClinic, Costa Rica-MS, Brazil; [2]Hospital Beneficência Portuguesa/ Beneficência Portuguesa Hospital, São José do Rio Preto-SP, Brazil. [3]Clinica Dottor's, Ambulatório Médico de Especialidade- AME, Clínica Prevencardio Exames/Dottor'sClinic, Ambulatory Medical Specialty Votuporanga e Jales-SP, Brazil. [4]Instituto MS-COR/MS-COR Institute, Catanduva-SP, Brazil [5]Clínica Pancor e Centro De Cardiologia Avançado/ Pancor Clinicandadvanced Cardiology Center - Santa Casa De Fernandópolis-SP, Brazil [6] Santa Casa Hospital, Lins-SP, Brazil [7]Ambulatório Médico de Especialidade-AME/ Ambulatory Medical Specialty Votuporanga-SP, Brazil [8]São José do Avai Hospital, Itaperuna/RJ, Brazil [9]Unimar Hospital, Marília-SP, Brazil; [10]Zotarelli-Filho ScientificWork, São José do Rio Preto/SP, Brazil. [11]FACERES - Medical SchoolofSao Jose do Rio Preto/SP, Brazil

ARTICLE INFO

Article History:
Received 20th July, 2020
Received in revised form
28th August, 2020
Accepted 19th September, 2020
Published online 30th October, 2020

Key Words:
COVID-19. SARS-CoV-2. Cardiovascular disease. Pharmacological treatments.

Corresponding author:
Fábio Morato de Oliveira

ABSTRACT

Introduction: In the new coronavirus (SARS-CoV-2) scenario, COVID-19 disease is associated with vascular inflammatory processes, myocarditis, and cardiac arrhythmias, thus, its mortality is associated with cardiovascular diseases (CVD), diabetes, and hypertension. The mechanisms are that cardiovascular disease and pharmacological inhibition of SARS-CoV-2 can increase ACE2 levels, and coronavirus infection can decrease ACE2. Among patients with COVID-19, there is a high prevalence of cardiovascular disease and over 7% of patients have a myocardial injury from infection (22% of critically ill patients). **Objective:** Therefore, the present study aimed to conduct a systematic review of the main clinical outcomes of cardiovascular effects in patients infected with COVID-19. **Methods:** Literary search criteria were followed with the use of the MeSH Terms that were cited in the item on "Search strategies". A total of 65 clinical studies that were submitted to the eligibility analysis were checked, and after that, 31 studies were selected. The search strategy was performed in PubMed, Embase, Ovid and Cochrane Library, Web of Science, Science Direct Journals (Elsevier), Scopus (Elsevier), OneFile (Gale). **Major considerations and conclusion:** Therefore, patients with COVID-19 combined with cardiovascular disease are associated with an increased risk of mortality. Critical patients are characterized by fewer lymphocytes. A COVID-19 disease is associated with a high inflammatory load that can induce vascular inflammation, myocarditis, and cardiac arrhythmias. Thus, cardiovascular risk factors and conditions must be carefully controlled according to the evidence-based guidelines. Cardiovascular disease and COVID-19 pharmacological inhibition increase ACE2 levels, which can increase coronavirus virulence in the lung and heart (7). On the other hand, there is evidence that coronavirus infection can decrease ACE2, leading to toxic over-accumulation of angiotensin II, which induces acute respiratory distress syndrome and fulminant myocarditis. The inhibition of SARS-CoV-2 can reduce this effect.

Citation: ***Otávio Queiroz Assumpção, Vanessa Piovesan Freitas Assumpção, Pedro WagnerRamos Júnior et al.*** "Sars-cov-2 andcardiovascular diseases: major considerations and systematic review*", International Journal of Development Research*, 10, (09), 41595-41599.

INTRODUCTION

In the scenario of the new coronavirus (SARS-CoV-2), the disease COVID-19 is associated with vascular inflammatory processes, myocarditis, and cardiac arrhythmias, thus, its mortality is associated with cardiovascular diseases, diabetes, and hypertension. These disorders share the underlying pathophysiology related to the renin-angiotensin system (RAS) (WHO, 2020) In this context, there are four different mechanisms that can contribute to increasing the virulence of the coronavirus in the lung and heart. Thus, the mechanisms are that cardiovascular disease and RAS pharmacological

inhibition can increase ACE2 levels, and coronavirus infection can decrease ACE2, leading to excess toxic accumulation of angiotensin II, which induces respiratory distress syndrome acute and fulminant myocarditis (WHO, 2020). Among patients with COVID-19, there is a high prevalence of cardiovascular disease and over 7% of patients have a myocardial injury due to infection (22% of critically ill patients) (Rodriguez-Morales, 2020). Although the angiotensin-converting enzyme 2 serves as a portal for infection, the role of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers requires further investigation. COVID-19 represents a challenge for heart transplantation, affecting donor selection, immunosuppression, and post-transplant management. There are a number of promising therapies under active investigation to treat and prevent COVID-19 (Wenzhong, liu, 2020). As an example, in order to know the incidence of these effects, as well as the care to be taken, a meta-analysis study carried out a systematic review of the literature followed by a meta-analysis, using three databases to assess clinical, laboratory, images, and results of confirmed cases with COVID-19. For 656 patients, fever (88.7%, 95% CI 84.5-92.9%), cough (57.6%, 40.8-74.4%) and dyspnea (45.6%, 10.9 -80.4%) were the most prevalent manifestations. Among the patients, 20.3% (95% CI 10.0-30.6%) required an intensive care unit (ICU), 32.8% had acute respiratory distress syndrome (ARDS) (95% CI 13.7- 51.8), 6.2% (95% CI 3.1 -9.3) with shock. Approximately 13.9% (95% CI 6.2-21.5%) of hospitalized patients had fatal results. COVID-19 places an enormous burden on health services, especially in patients with comorbidities. The ICU was necessary for approximately 20% of polymorphic patients infected with COVID-19 (Clerkin, 2020). Therefore, the present study aimed to conduct a systematic review of the main clinical outcomes of cardiovascular effects in patients infected with COVID-19.

METHODS

Eligibility and Study Design: Literary search criteria were followed with the use of the MeSH Terms that were cited in the item on "Search strategies". A total of 65 clinical studies that were submitted to the eligibility analysis were checked, and after that, 31 studies were selected, following the rules of systematic review-PRISMA (Transparent reporting of systematic reviews and meta-analysis-http: //www.prisma-statement.org/) (Figure 1).

Search Strategy and Information Sources: The search strategy was performed in PubMed, Embase, Ovid and Cochrane Library, Web of Science, ScienceDirect Journals (Elsevier), Scopus (Elsevier), OneFile (Gale) followed the following steps: - search for MeSHTerms:"COVID-19. SARS-CoV-2. Cardiovascular disease. Pharmacological treatments", and use of boolean "and" between mesh terms and "or" among historical findings. All references are registered in EndNote.

DEVELOPMENT AND DISCUSSION

In the scenario of cardiovascular diseases (CVD), this was common comorbidity in patients with COVID-19 (5,6). In SARS-CoV-2, the prevalence of diabetes mellitus (DM) (MD) and CVD was 11% and 8%, respectively, increasing the risk of death by 12 times (5-8). In 1 cohort of 191 patients from Wuhan, China, any comorbidity was present in 48% (67% of non-survivors), hypertension in 30% (48% of non-survivors), DM in 19% (31% of non-survivors), and CVD in 8% (13% of non-survivors) (Zhou, 2020).

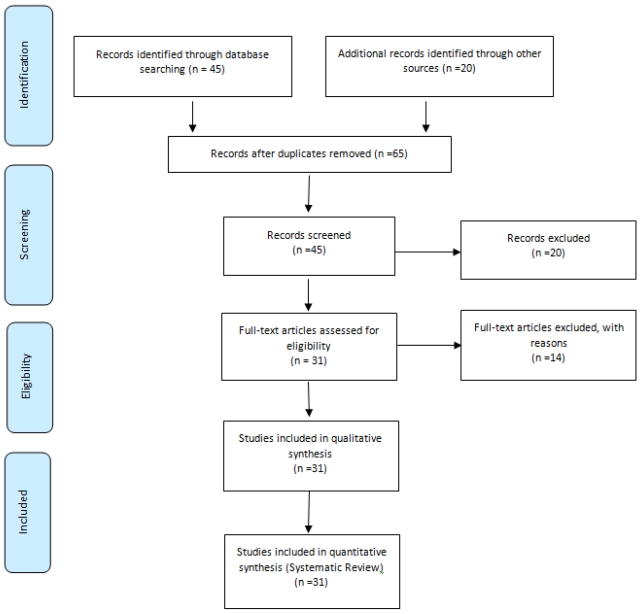

Figure 1. Flow chart. Eligibility of studies

In a cohort of 138 patients hospitalized with COVID-19, comorbidities were similarly prevalent (46% overall and 72% in patients requiring care in the intensive care unit (ICU), as well as cardiovascular comorbidities: hypertension in 31% (58% in patients requiring ICU care), CVD in 15% (25% in patients requiring ICU care) and DM in 10% (22% in patients requiring ICU care) (Wang, 2020). Still, an analysis of an outpatient and inpatient cohort of 1,099 patients with COVID-19 revealed that 24% had some comorbidity (58% among those with intubation or death), with 15% having hypertension (36% among those with intubation or death), 7.4% DM (27% among those with intubation or death) and 2.5% of coronary heart disease (9% among those with intubation or death) (Guan, 2019). In this context, data from the China National Health Commission demonstrated that 35% of patients diagnosed with COVID-19 had hypertension and 17% had coronary disease (Zheng, 2020). A recent meta-analysis of 8 studies from China including 46,248 infected patients showed that the most prevalent comorbidities were hypertension (Yang, 2020). Possible explanations include CVD being more prevalent in patients with advanced age, and immune system with functional deficiency or high levels of ACE2 or patients with CVD who are predisposed to COVID-19.

In this sense, myocardial injury is evidenced by elevated cardiac biomarkers. In the aforementioned study of 138 patients hospitalized with COVID-19 in Wuhan, China, cardiac injury (highly sensitive cardiac troponin I (hs-cTnI) or new echocardiographic abnormalities) was present in 7.2% of patients in general and 22% of patients who needed ICU care (Wang, 2020). The report by the National Health Commission of China reported that almost 12% of patients with no known CVD had elevated levels of troponin or cardiac arrest during hospitalization (Zheng, 2020). As a consequence, hs-cTnI was above the upper reference limit of the 99th percentile in 46% of non-survivors, as opposed to 1% of survivors (Zhou, 2020). In this regard, there are two patterns of myocardial injury with COVID-19. Thus, a study demonstrated that four days after the

onset of symptoms, the mean levels of hs-cTnI were 8.8 pg/mL in non-survivors versus 2.5 pg/mL in survivors. During follow-up, the median hs-cTnI among survivors did not change significantly (2.5 to 4.4 pg/mL), while it rose to 24.7 pg/mL on day 7, to 55.7 pg/mL in the day 13, to 134.5 pg/ml on day 19 and 290.6 pg/ml on day 22 in non-survivors. The average time to death since the onset of symptoms was 18.5 days (interquartile range, 15 to 20 days). The increase in hs-cTnI range with other inflammatory biomarkers (D-dimer, ferritin, interleukin-6, lactate dehydrogenase), raising the possibility that this reflects a cytokine storm or secondary hemophagocyticlymphohistiocytosis more than isolated myocardial injury. In contrast, reports from patients with predominantly cardiac symptoms suggest a different pattern, potentially viral myocarditis or stress cardiomyopathy. For example, 1 case recently published described a man with chest pain and ST-segment elevation on his echocardiogram(ECG), but without coronary obstruction. An ECG observed left ventricular dysfunction (ejection fraction 27%, left ventricular end-diastolic diameter 5.8 cm) and elevated cardiac biomarkers (troponin T> 10 ng/mL, NT-proBNP (N-terminal pro-BNP)> 21,000 pg / ml) (Hu, 2020). In China, one report showed a 63-year-old man with no cardiac history, who had severe respiratory manifestation and evidence of fulminant myocarditis with an enlarged left ventricle (left ventricular end-diastolic diameter 6.1 cm) and depressed left ventricular function (ejection fraction 32%). The patient had elevated troponin I (> 11 ng/mL) and NT-proBNP (> 22,000 pg/mL). Given the severity of the cardiogenic shock, he was placed on extracorporeal membrane oxygenation and treated with intravenous immunoglobulin, steroids, antiviral therapy, and renal replacement therapy. The patientrecovered ventricular function in 2 weeks (Zeng, 2020). The World Health Organization and the Centers for Disease Control and Prevention do not recommend the use of glucocorticoids, except for chronic obstructive pulmonary disease or exacerbation of asthma (Centers for Disease Control and Prevention, 2020; World Health Organization, 2020). The exact mechanism of cardiac involvement in COVID-19 remains under investigation (Oudit, 2009). A potential mechanism is direct myocardial involvement mediated by ACE2. Among humans, during the coronavirus outbreak in Toronto, SARS-CoV viral RNA was detected in 35% of autopsied hearts (Booth, 2003). COVID-19-related cardiac involvement includes a cytokine storm, mediated by an unbalanced response between helper T cell subtypes, and hypoxia-induced excessive intracellular calcium, leading to cardiac myocyte apoptosis (Zhou, 2020; Zheng, 2020).

In the context of ACE2, the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers is common in cardiovascular disorders (hypertension, coronary artery disease, congestive heart failure, and DM). However, conflicting data exist on whether these drugs increase (Ishiyama, 2004; Ferrario, 2005; Ocaranza, 2006) or have a minimal effect on ACE2 levels (Klimas et al., 2015; Walters, 2017; Burchill, 2012; Burrell, 2005). The entry of SARS-CoV-2 into cells is dependent on ACE2, however, ACE2 appears to have a protective function against acute lung injury (Imai, 2005; Kuba, 2005). In this regard, Losartan is being studied for potential mitigation of lung injury among hospitalized and outpatients with COVID-19 (Randomized Controlled Trial of Losartan for Patients, 2020; Randomized Controlled Trial of Losartan for Patients). The use of angiotensin-converting enzyme inhibitor and angiotensin receptor blockers (ACEI and ARB) does not affect the morbidity and mortality of COVID-19 combined with CVD. Aggravating causes of death include fulminant inflammation, accumulation of lactic acid, and thrombotic events (Peng, 2020). Therefore, patients with COVID-19 combined with cardiovascular disease are associated with an increased risk of mortality. Critical patients are characterized by fewer lymphocytes. Higher BMI is more often seen in critically ill, non-survivors. The use of ACEI / ARB does not affect the morbidity and mortality of COVID-19 combined with CVD. Aggravating causes of death include fulminant inflammation, accumulation of lactic acid, and thrombotic events. Therefore, cardiovascular metabolic comorbidities made patients more susceptible to COVID-19 and exacerbated the infection (Peng, 2020). Finally, a multicenter, open, randomized, controlled clinical study evaluated the efficacy and safety of hydroxychloroquine plus standard treatment compared to standard treatment alone in adults with COVID-19 (Tang, 2019). Sixteen government-designated COVID-19 treatment centers in China from 11 to 29 February 2020. 150 patients admitted to the hospital with laboratory-confirmed COVID-19 were included in the intention to treat analysis (75 patients designated for hydroxychloroquine plus treatment 75 for standard treatment only). Hydroxychloroquine is administered at a loading dose of 1200 mg per day for three days, followed by a maintenance dose of 800 mg per day (total duration of treatment: two or three weeks for patients with mild to moderate or severe illness, respectively). Of 150 patients, 148 had mild to moderate illness, and two had severe illness. The average duration from symptom onset to randomization was 16.6 (SD 10.5; range 3-41) days. A total of 109 (73%) patients (56 standard treatment; 53 standard treatment plus hydroxychloroquine) had negative conversion well before 28 days, and the remaining 41 (27%) patients (19 standard treatment; 22 standard treatment) plus hydroxychloroquine) were censored because they did not achieve negative virus conversion. The probability of negative conversion in 28 days in the standard treatment plus hydroxychloroquine group was 85.4% (95% confidence interval 73.8% to 93.8%), similar to the standard treatment group (81.3 %, 71.2% to 89.6%). The most common adverse event in hydroxychloroquine receptors was diarrhea, reported in 7/70 (10%) patients. Two hydroxychloroquine receptors reported serious adverse events (Tang, 2019).

Conclusion

Therefore, COVID-19 disease is associated with a high inflammatory load that can induce vascular inflammation, myocarditis, and cardiac arrhythmias. Thus, cardiovascular risk factors and conditions must be carefully controlled according to the evidence-based guidelines. Cardiovascular disease and COVID-19 pharmacological inhibition increase ACE2 levels, which can increase coronavirus virulence in the lung and heart (Booth, 2003). On the other hand, there is evidence that coronavirus infection can decrease ACE2, leading to toxic over-accumulation of angiotensin II, which induces acute respiratory distress syndrome and fulminant myocarditis. The inhibition of SARS-CoV-2 can reduce this effect.

Declaration of Potential Conflict of Interest: The authors declare no conflict of interest.

Funding: Not applicable

Data sharing statement: No additional data are available

REFERENCES

Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis.Int J Infect Dis. 2016; 49:129–133. doi: 10.1016/j.ijid.2016.06.015Crossref Medline Google Scholar

Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, Walmsley SL, Mazzulli T, Avendano M, Derkach P, et al.. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area.JAMA. 2003; 289:2801–2809. doi: 10.1001/jama.289.21. JOC30885 Crossref Medline Google Scholar

Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, Walmsley SL, Mazzulli T, Avendano M, Derkach P, et al.. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area.JAMA. 2003; 289:2801–2809. doi: 10.1001/jama.289.21. JOC30885 Crossref Medline Google Scholar

Burchill LJ, Velkoska E, Dean RG, Griggs K, Patel SK, Burrell LM. Combination renin-angiotensin system blockade and angiotensin-converting enzyme 2 in experimental myocardial infarction: implications for future therapeutic directions.ClinSci (Lond). 2012; 123:649–658. doi: 10.1042/CS20120162CrossrefMedlineGoogle Scholar

Burrell LM, Risvanis J, Kubota E, Dean RG, MacDonald PS, Lu S, Tikellis C, Grant SL, Lew RA, Smith AI, et al.. Myocardial infarction increases ACE2 expression in rat and humans.Eur Heart J. 2005; 26:369–375; discussion 322. doi: 10.1093/eurheartj/ehi114CrossrefMedlineGoogle Scholar

Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19).https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html. Revised March 7th, 2020. Accessed March 21, 2020. Google Scholar

Chan JW, Ng CK, Chan YH, Mok TY, Lee S, Chu SY, Law WL, Lee MP, Li PC. 2003. Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS).Thorax. 58:686–689. doi: 10.1136/thorax.58.8.686.

Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, Jain SS, Burkhoff D, Kumaraiah D, Rabbani L, Schwartz A, Uriel N. 2020. COVID-19 and Cardiovascular Disease. Circulation. 2020 May 19;141(20):1648-1655. doi: 10.1161/CIRCULATIONAHA.120.046941. Epub Mar 21. PMID: 32200663.

Ferrario CM, Jessup J, Chappell MC, Averill DB, Brosnihan KB, Tallant EA, Diz DI, Gallagher PE. 2005. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation. 111:2605–2610. doi: 10.1161/CIRCULATIONAHA.104.510461LinkGoogle Scholar

Guan W-j, Ni Z-y, Hu Y, Liang W-h, Ou C-q, He J-x, Liu L, Shan H, Lei C-l, Hui DSC, et al. 2020. Clinical characteristics of coronavirus disease 2019 in China (published online February 28, 2020).N Engl J Med. doi: 10.1056/NEJMoa2002032.

Hu H, Ma F, Wei X, Fang Y. 2020. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin (published online March 16,). Eur Heart J. doi: 10.1093/eurheartj/ehaa190. https://academic.oup.com/eurheartj/article/doi/10.1093/eurheartj/ehaa190/5807656 Google Scholar

Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, Yang P, Sarao R, Wada T, Leong-Poi H, et al.. Angiotensin-converting enzyme 2 protects from severe acute lung failure.Nature. 2005; 436:112–116. doi: 10.1038/nature03712 Crossref Medline Google Scholar

Ishiyama Y, Gallagher PE, Averill DB, Tallant EA, Brosnihan KB, Ferrario CM. 2004. Upregulation of angiotensin-converting enzyme 2 after myocardial infarction by blockade of angiotensin II receptors. Hypertension.; 43:970–976. doi: 10.1161/01.HYP.00001 24667.34652.1a Link Google Scholar

Klimas J, Olvedy M, Ochodnicka-Mackovicova K, Kruzliak P, Cacanyiova S, Kristek F, Krenek P, Ochodnicky P. Perinatally administered losartan augments renal ACE2 expression but not cardiac or renal Mas receptor in spontaneously hypertensive rats.J Cell Mol Med. 2015; 19:1965–1974. doi: 10.1111/jcmm.12573CrossrefMedlineGoogle Scholar

Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, Huan Y, Yang P, Zhang Y, Deng W, et al.. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury.Nat Med. 2005; 11:875–879. doi: 10.1038/nm1267CrossrefMedlineGoogle Scholar

Ocaranza MP, Palomera C, Román M, Bargetto J, Lavandero S, Jalil JE. Effect of hypertension on angiotensin-(1-7) levels in rats with different angiotensin-I converting enzyme polymorphism.Life Sci. 2006; 78:1535–1542. doi: 10.1016/j.lfs.2005.07.026CrossrefMedlineGoogle Scholar

Oudit GY, Kassiri Z, Jiang C, Liu PP, Poutanen SM, Penninger JM, Butany J. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS.Eur J Clin Invest. 2009; 39:618–625. doi: 10.1111/j.1365-2362.2009.02153.xCrossrefMedlineGoogle Scholar

Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, He MA, Cheng LX, Huang K, Zeng QT. 2019. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. ZhonghuaXinXueGuan Bing ZaZhi. 2020 Mar 2;48(0):E004. doi: 10.3760/cma.j.cn112148-20200220-00105.

Randomized Controlled Trial of Losartan for Patients With COVID-19 Not Requiring Hospitalization. Clinical Trials.gov identifier: NCT04311177. https://clinicaltrials.gov/ct2/show/NCT04311177. March 17,2020. Accessed March 21, 2020.Google Scholar

Randomized Controlled Trial of Losartan for Patients With COVID-19 Requiring Hospitalization.ClinicalTrials.gov identifier: NCT04312009. https://clinicaltrials.gov/ct2/show/NCT04312009. March 17, 2020. Accessed March 21, 2020.Google Scholar

Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JP, Alvarado-Arnez LE, Bonilla-Aldana DK, Franco-Paredes C, Henao-Martinez AF, Paniz-Mondolfi A, Lagos-Grisales GJ, Ramírez-Vallejo E, Suárez JA, Zambrano LI, Villamil-Gómez WE, Balbin-Ramon GJ, Rabaan AA, Harapan H, Dhama K, Nishiura H, Kataoka H, Ahmad T, Sah R; Latin American Network of Coronavirus Disease 2019-COVID-19 Research

(LANCOVID-19).Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. Travel Med Infect Dis. 2020 Mar 13:101623. doi: 10.1016/j.tmaid.2020.101623.

Tang W, Cao Z, Han M, Wang Z, Chen J, Sun W, Wu Y, Xiao W, Liu S, Chen E, Chen W, Wang X, Yang J, Lin J, Zhao Q, Yan Y, Xie Z, Li D, Yang Y, Liu L, Qu J, Ning G, Shi G, Xie Q. 2020. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial.BMJ. 2020 May 14;369:m1849. doi: 10.1136/bmj.m1849. PMID: 32409561; PMCID: PMC7221473.

Walters TE, Kalman JM, Patel SK, Mearns M, Velkoska E, Burrell LM. 2017. Angiotensin converting enzyme 2 activity and human atrial fibrillation: increased plasma angiotensin converting enzyme 2 activity is associated with atrial fibrillation and more advanced left atrial structural remodelling.Europace. 2017; 19:1280–1287. doi: 10.1093/europace/euw246MedlineGoogle Scholar

Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, et al. 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China.JAMA. 2020; 323:1061–1069. doi: 10.1001/jama.2020.1585 Crossref Medline Google Scholar

Wenzhong, liu;hualan, Li 2020. COVID-19: Attacks the 1-Beta Chain of Hemoglobin and Captures the Porphyrin to Inhibit Human Heme Metabolism. ChemRxiv. Preprint. https://doi.org/10.26434/chemrxiv.11938173.v7.

WHO-World Health Organization. Available in: https://www.paho.org/bra/index.php?option=com_content&view=article&id=5253:doencas-cardiovasculares&Itemid=1096. Accessed May 27, 2020.

World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected.https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. Published March 13,2020. Accessed March 21, 2020.Google Scholar

Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y. 2020. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis (published online March 12, 2020).Int J Infect Dis. doi: 10.1016/j.ijid.2020.03.017. https://www.sciencedirect.com/science/article/pii/S1201971220301363Google Scholar

Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, Wang LF, Gao H, Wang Y, Dong CF, et al. 2020. First case of COVID-19 infection with fulminant myocarditis complication: case report and insights.preprints. 2020; 2020030180. doi: 10.20944/preprints202003.0180.v1Google Scholar

Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. 2020. COVID-19 and the cardiovascular system (published online March 5, 2020).Nat Rev Cardiol. doi: 10.1038/s41569-020-0360-5. https://www.nature.com/articles/s41569-020-0360-5Google Scholar

Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.Lancet. 395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3Crossref Medline Google Scholar

****