Heart in patients infected
With 2019 Novel Coronavirus (Covid-19)

Abdallah FAYSSOIL, MD, (1, 2)
Benjamin DAVIDO, MD, (3)
Hazrije MUSTAFIC, MD, PhD, (2, 4)
Aurélien DINH, MD, (3)
Nicolas MANSENCAL, MD, PhD, (2, 4)

1) Unité de cardiologie, CHU Raymond Poincaré, APHP, Garches, France
2) Department of Cardiology, Ambroise Paré Hospital, Assistance Publique-Hôpitaux de
   Paris (AP-HP), Centre de référence des cardiomyopathies et des troubles du rythme
   cardiaque héréditaires ou rares, Université de Versailles-Saint Quentin (UVSQ),
   Boulogne-Billancourt, France
3) Service de maladies infectieuses, CHU Raymond Poincaré, APHP, Garches, France
4) INSERM U-1018, CESP, UVSQ, Villejuif, France

Corresponding Author:
Abdallah FAYSSOIL, MD
Raymond Poincare Hospital, APHP, Garches, France
E-mail: abdallah.fayssoil@aphp.fr
Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an emerging infectious disease with currently a pandemic state. Cardiac function can be involved, affecting prognosis, in addition with lung feature severity, particularly in patients with comorbidities. Since the renin angiotensin aldosterone (RAA) system may interact with SARS-Cov-2, researches are still ongoing to assess the prognostic value of RAA blockers in cardiology.

Word counts: 2195

Key words: coronavirus; heart; prognosis; COVID-19; ICU
Introduction

In December 2019, a subset of clusters of unknown pneumonia cases emerged in Wuhan, Hubei Province (China). This unknown pneumonia onset was found to be linked to a local seafood wholesale market (1). It was found to be due to a novel beta-coronavirus, namely the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2, 3). This novel coronavirus was identified by the Chinese Center for Disease Control and Prevention (CDC) on 7 January 2020, named 2019-nCoV by the World Health Organization (WHO)(4) and thereafter COVID-19. This emerging disease, rapidly, spread out of China, reaching other Asian countries, the USA (5) and the Europe (6) through Italy, with currently a global pandemic state, declared on March 11, 2020 by the WHO (4). Confirmed COVID-19 cases reached the number 1,924,878 persons over the world the 14th of April 2020 (7). In many countries, governments decided plans to include quarantine measures in order to modify the epidemic curve and to slow the pandemic (8). Clinical presentation of infected patients ranges from asymptomatic status to severe pneumonia (2, 3). Currently, it appears that 81% of people with COVID-19 infection disclose a mild disease. Cardiac comorbidities are often present in patients with severe COVID-19 infection (9). Cardiac injury may occur in patients infected with COVID 19 (3) and affects the prognosis (10). Also, the renin angiotensin-aldosterone system seems to interact with the Covid-19 lung infection process, especially ACE2 receptors, which would allow the virus to particularly entry in the pulmonary level, arguing the discontinuation of angiotensin converting enzyme (ACE) inhibitors drugs or angiotensin receptors blockers (ARB) in patients with cardiovascular diseases.

We aimed to review the cardiac features among patients suffering from COVID-19 infection as well as its prognosis.
Clinical characteristics and biological features in patients with Covid-19

After an incubation period, in patients presenting with symptoms, the most common clinical manifestations are fever (83-98.6%), cough (59%-79%), dyspnea (31%-63.5%), asthenia (23%-69%), myalgia (11%-35%), gastrointestinal disorders (1%-10%), headache (6.5%-8%) (3, 11, 12, 13). Some patients may require hospitalization and a subset of patients (about one third) (2, 3) need admission in intensive care unit (ICU) because of a severe respiratory failure. In ICU wards, complications include acute respiratory failure, acute respiratory distress syndrome (ARDS) (14), cardiac injury and death (11). In the study by Chen et al (11), 75% and 17% of patients disclosed bilateral pneumonia and ARDS, respectively. The median time from first symptoms to hospital admission was globally reported to be around 7 days (3), whereas the median duration from onset of symptoms to ICU admission was reported to be at 9.5 days (15). Biological results are classically disturbed with reduced total lymphocytes, elevated lactate dehydrogenase and prolonged prothrombin time (3). The following blood abnormalities have been found in ICU patients (3): an increase of cardiac troponin I, creatinine, urea nitrogen, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, total bilirubin, creatine kinase and a decrease of white blood cell counts. Lymphopenia is common in infected patients, from 40% to 83% (9, 12, and 13). Hepatitis is common with an increase of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and lactate dehydrogenase. D-dimers are classically increased with a coagulopathy state, reaching 34% (10).

Diagnosis of COVID-19 pneumonia relies on nasopharyngeal swab specimen or bronchial aspirates, using real time reverse –transcriptase-polymerase-chain –reaction assay (RT-PCR). Plasma can also be used to detect coronavirus (16). In addition, CT chest is commonly used to
precise extension and severity of the pneumonia and support the diagnosis in case of negative RT-PCR (17).

**Thoracic Imaging findings**

Thoracic imaging reveals usually COVID 19 features characteristics in pneumonia-infected patients. These impairments are due to lung damages, caused by the SARS-COV2. It has been reported with lung histological studies, diffuse alveolar damages, pulmonary edema, and interstitial mononuclear inflammatory infiltrates (15). Ground glass opacities, bilateral patchy shadow and areas of consolidation ([figure 1](#)) are classical findings in thoracic computed tomography (CT) scans (3). In the study by Yang et al (13), the median duration from onset of symptoms to radiological confirmation of pneumonia was 5 days. Ground glass opacities were found in 48%-56.4% of patients and 52%-75% of patients disclosed bilateral reticular nodular opacities on chest X ray (9, 11, 18). In ICU, 100% of patients presented with bilateral involvement on chest X ray (2). Lung ultrasound ([figure 2](#)) can also be used to assess lung involvement and severity, searching for diffuse B lines, particularly in patients with thoracic scan unavailability (19).

**Cardiac features in COVID - 19 infected patients**

Cardiovascular comorbidities are often present in patients infected with COVID 19. In the study by Zhou *et al* (13), comorbidities were present in 48% of patients, mainly arterial hypertension, diabetes and coronary artery disease. It should be noted that smoking is associated with an increase of ACE2 binding with Covid-19 and might explain why those comorbidities are usually encountered in severe clinical presentation of covid-19 in those patients (20). Also COVID19 classically affects more male rather than female, possibly because of a different background and susceptibility (11). In the study by Wang *et al* (3) that
included ICU patients, a history of hypertension was found in 58% of patients, 25% of patients had a history of cardiovascular diseases, and diabetes, history of cerebrovascular diseases and chronic kidney disease were present in 22%, 16.7% and 5.6% of patients, respectively. In two previous studies (2, 11), cardiovascular diseases were present in 15% and 40% of patients. In the study by Bhatraju et al (21), diabetes mellitus was present 58% of patients, obstructive sleep apnea in 21% of patients and chronic kidney disease in 21% of patients. In a large study including 1591 ICU patients (aged around 63 years) admitted in the Lombardy Region in Italy (22) arterial hypertension was present in 49% of patients, cardiovascular diseases in 21% of patients and 17% of patients have a history of diabetes.

In the meantime, cardiac injury has been found to be frequent in patients with COVID-19 pulmonary infection and this feature affects prognosis. In general, in patients with pneumonia, the risk factors for cardiac events include preexisting cardiac diseases, older age and pneumonia severity (23). In the study by Chen et al (11), that included 99 patients (age 55.5 years) with COVID 19 pneumonia, 2% of patients disclosed chest pain. In the study by Zhou et al (13), non-survivor’s patients had a history of arterial hypertension (48%), diabetes (31%) and coronary disease (24%). Heart failure is significantly present in non-survivor patients (p<0.0001) and acute cardiac injury, defined as an increase of cardiac biomarkers (high-sensitivity cardiac troponin I) or new electrocardiographic and echocardiographic abnormalities (13). Acute cardiac injury occurred in 22% of ICU patients vs 2% in non-ICU patients (p<0.001) (3). In 21 critically ill patients (aged around 70 years old) with COVID 19 (18), cardiomyopathy occurred in 33% of patients. Brain-type natriuretic peptide level was elevated, 4720 pg/ml, as well as troponin level (3ng/ml) (18). In the study by Guo et al (10), 27.8% disclosed cardiac injury and this feature is significantly associated with mortality. Cardiac injury is frequently found in patients hospitalized in ICU, from 19.7% to 31% (2,13,24).This feature was particularly present in older patients, patients with comorbidities
(hypertension 59.8%), higher levels of C-reactive protein, procalcitonin, creatine kinase – myocardial band, myohemoglobin, high-sensitivity troponin I, N-terminal pro-B-type natriuretic peptide, higher leukocytes counts, creatinine, aspartate aminotransferase, higher radiologic involvement (ground-glass opacity) (24). Ruan Q et al (25) reported also myocarditis among 68 deaths in a case series of 150 patients with COVID-19, where 7% were associated with myocarditis with circulatory failure. It has been found a relationship between the pulmonary severity and the cardiac injury (3). In ICU patients, admitted because of hypoxemic respiratory failure, Bhatraju et al (21), reported troponin increase in 15% of patients. Dyspnea is also a classical feature in patients, mainly in relation with lung injury. In the study by Huang et al (1), dyspnea was present in 55% of patients and time from illness onset to dyspnea was at 8 days. The median time from illness onset to dyspnea onset was 13 days, in the study by Zhou et al (12). Acute pulmonary embolism may be present in COVID 19 infected patients, without clear causal relationship (26). Finally, in ICU, hemodynamic features are frequent and vasoconstrictive agents were used in 35% of critically ill patients (13). In addition with cardiac injury, arrhythmia may occur in COVID 19 infected patients (3). Sudden cardiac arrests have also been reported (15). Arrhythmia occurred in 44% of ICU COVID -19 patients vs 6.9% in non-ICU COVID-19 patients (p<0.001) (3). Ventricular fibrillation/ventricular tachycardia (VF/VT) occurred in 5.9% of patients and increased troponin was associated with onset of VF/VT (17.3%) (10).

In summary, risk factors for cardiac injury (2, 10, 13, 18, and 24) are as follows: older age, hypertension, cardiovascular diseases, cardiomyopathy, diabetes, chronic kidney diseases. The table 1 summarizes principal studies in infected COVID 19 patients, associated with cardiac injury.
Renin angiotensin aldosterone system and Covid -19

Cardiac comorbidities are thus frequent in patients with Covid-19 (9, 27). Angiotensin converting enzyme (ACE) inhibitors and ARB are commonly prescribed in patients with hypertension, chronic heart failure and diabetes. The renin angiotensin system (RAA) may interact with the COVID 19 infection process (28, 29). Indeed, ACE 2 is an enzyme present in the lung epithelial cells and is functionally as a receptor for SARS Cov2 (30). Physiologically, the ACE 2 degrades angiotensin 2 to angiotensin (1-7), reducing, in the way, fibrosis and vasoconstriction (29). Since ACE 1 inhibitors and ARB increase ACE 2 activities, these drugs, in theory, may be harmful in patients infected with Covid 19 (31). Researches are needed to clarify mechanisms and outcomes in patients treated with RAA blockers. Currently, The European Society of Cardiology (ESC) as well as the American Heart Association recommends continuing these previous drugs, since there is no scientific evidence to discontinue ACE inhibitors or ARB in patients with Covid -19 infection (32, 33). However, the community is still investigating if there is a clear association between COVID-19 mortality and the renin-angiontensin system (34).

Cardiac features, ARDS, prognosis and mortality

The table 2 summarizes risk factors associated with mortality in COVID-19 infected patients. In patients infected with COVID 19, the onset of cardiac injury and the association between cardiac injury and onset of ARDS affects prognosis (13, 24). Mortality rate dramatically increases in case of previous cardiovascular diseases, comorbidities and in ICU patients (13, 35). Older age is also a significant factor for ICU mortality, reaching up to 67% in patients older than 70 years (18).

In critically ill patients, mortality may reach 61% (13, 21). In the study by Arentz et al (18), that included ICU patients with a mean age of 70 years, in the Washington state,
cardiomyopathy occurred in 33% of patients and vasopressors were used in 67% of patients. In the study by Zhou et al (12), that included 191 patients (median age: 56 years), non-survivor patients disclosed high sensibility cardiac troponin I (p<0.00001). Zhou et al (12), using multivariate regression, found that in-hospital mortality was associated with older age (OR 1.1), higher sequential organ failure assessment (SOFA) score (OR 5.6) and d-dimer >1 μg/mL (OR 18.4) at admission. Also, the mortality group disclosed sepsis (p<0.0001), respiratory failure (p<0.0001), ARDS (p<0.0001), coagulopathy (p<0.0001), acute kidney injury (p<0.0001), acidosis (p<0.0001) and ICU admission (p <0.0001). In the study by Shio et al (24), patients with cardiac injury mostly require mechanical ventilation and have complications that include ARDS, acute kidney injury, hypoproteinemia, coagulation disorders and electrolytes disturbances. Using multivariate Cox regression, they found that cardiac injury (HR=3.4, p 0.001) and ARDS (HR 7.11, p<0.001) were associated with mortality (24). Increased troponin is a major marker of mortality (10): 59.6% versus 8.9% without elevated troponin (p<0.001). Whatever the rate of mortality in studies, patients with previous cardiovascular disease have a worst prognosis. In the study by Wu et al (36), mortality was 10.5% in patients with cardiovascular disease versus 2.3% without cardiovascular disease. In the recent Italian study including 1591 ICU patients (mean age: 63 years old), ICU mortality was at 26% and affects mainly older man (age ≥ 64 years) (22) and prevalence of hypertension was higher in patients died in ICU (p<0.001) (22).

Acute respiratory distress syndrome (ARDS) is present in 67% of patients in critically ill patients and is a major cause of mortality (2, 3, 13, 18, and 35). In the study by Wu et al (27), which included 201 patients (mean age: 51 years), ARDS occurred in 41.8% of patients. The following parameters were found to predict the onset of ARDS: older age, neutrophilia, organ and coagulation dysfunction.
Acute kidney failure is another complication in ICU patients: from 8 to 29% (2, 3, 13, 18) and renal replacement therapy may be used in 17% of patients (13). Thus, this is a frequent complication of Covid-19 that affects the prognosis of our patients.

**Conclusion**

COVID-19 spares no organ including heart, as other major virus. Better identify patients at risk of cardiovascular failure may help to reduce mortality induced by physiological stress and adjust cardiological drugs. Also, those patients might be subject to a subsequent episode of cardiac dysfunction after discharge and should be particularly followed-up.

*Conflicts of interest: none*
References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb 20;382(8):727-733.

2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506.

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 Feb 7.

4. Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020 Mar 19;91(1):157-160.

5. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkerson S, Tural A, Diaz G, Cohn A, Fox L, Patel A, Gerber SI, Kim L, Tong S, Lu X, Lindstrom S, Pallansch MA, Weldon WC, Biggs HM, Uyeki TM, Pillai SK; Washington State 2019-nCoV Case Investigation Team. First Case of 2019 Novel Coronavirus in the United States. N Engl J Med. 2020 Mar 5;382(10):929-936.

6. Spiteri G, Fielding J, Diercke M, Campese C, Enouf V, Gaymard A, Bella A, Sognamiglio P, Sierra Moros MJ, Riutort AN, Demina YV, Mahieu R, Broas M, Bengnér M, Buda S, Schilling J, Filleul L, Lepoutre A, Saura C, Mailles A, Levy-Bruhl D, Coignard B, Bernard-Stoecklin S, Behillil S, van der Werf S, Valette M, Lena B,
Riccardo F, Nicastri E, Casas I, Larrauri A, Salom Castell M, Pozo F, Maksyutov RA, Martin C, Van Ranst M, Bossuyt N, Siira L, Sane J, Tegmark-Wisell K, Palmérus M, Broberg EK, Beauté J, Jorgensen P, Bundle N, Pereyaslov D, Adlhoch C, Pukkila J, Pebody R, Olsen S, Ciancio BC. First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. Euro Surveill. 2020 Mar;25(9).

7. Johns Hopkins University CSSE. Wuhan coronavirus (2019-nCoV) global cases (https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6. opens in new tab).

8. The Lancet Respiratory Medicine. COVID-19: delay, mitigate, and communicate. Lancet Respir Med. 2020 Mar 16.

9. 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. Guan WJ, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Feb 28.

10. Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Guo T, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020 Mar 27:e201017.

11. 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 Feb 15;395(10223):507-513.
12. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 11.

13. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020 Feb 24.

14. Ranieri VM, Rubenfeld GD, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012, 307(25), 2526-2533.

15. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020 Feb 18.

16. Zhang G, Zhang J, Wang B, Zhu X, Wang Q, Qiu S. Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a retrospective analysis. Respir Res. 2020 Mar 26;21(1):74.

17. Yicheng Fang, Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology. Published Online:Feb 19 2020.

18. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, Lee M. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 2020 Mar 19.

19. Peng QY, Wang XT, Zhang LN; Chinese Critical Care Ultrasound Study Group (CCUSG). Findings of lung ultrasonography of novel corona virus pneumonia during the 2019-2020 epidemic. Intensive Care Med. 2020 Mar 12
20. Brake SJ, Barnsley K, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking Upregulates Angiotensin-Converting Enzyme-2 Receptor: A Potential Adhesion Site for Novel Coronavirus SARS-CoV-2 (Covid-19). J Clin Med. 2020 Mar 20;9(3).

21. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, Greninger AL, Pipavath S, Wurfel MM, Evans L, Kritek PA, West TE, Luks A, Gerbino A, Dale CR, Goldman JD, O'Mahony S, Mikacenic C. Bhatraju PK, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. N Engl J Med. 2020 Mar 30.

22. Grasselli G, Zanirillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cerda D, Coluacello A, Foti G, Fumagalli R, Iotti G, Latronico N, Lorini L, Merler S, Natalini G, Piatti A, Ranieri MV, Scardoglio AM, Storti E, Cecconi M, Pesenti A; COVID-19 Lombardy ICU Network. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020 Apr 6.

23. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the cardiovascular system. Lancet, 381 (2013), pp. 496-505.

24. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B, Huang C. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA cardio 2020 Mar 25.

25. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020 Mar 3.

26. Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? Eur Heart J. 2020 Mar 30.

27. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, Huang H, Zhang L, Zhou X, Du C, Zhang Y, Song J, Wang S, Chao Y, Yang Z, Xu J, Zhou X, Chen D, Xiong W, Xu L, Zhou F,
Jiang J, Bai C, Zheng J, Song Y. Wu C, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020 Mar 13:e200994.

28. Guo J, Huang Z, Lin L, Lv J. Coronavirus Disease 2019 (COVID-19) and Cardiovascular Disease: A Viewpoint on the Potential Influence of Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers on Onset and Severity of Severe Acute Respiratory Syndrome Coronavirus 2 Infection. J Am Heart Assoc. 2020 Apr 7;9(7):e016219

29. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med. 2020 Mar 30.

30. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. Hoffmann M, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020 Mar 4.

31. Aronson JK, Ferner RE. Drugs and the renin-angiotensin system in covid-19. BMJ. 2020 Apr 2;369:m1313.

32. De Simone G. Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers.2020.

33. American Heart Association. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19. Accessed March 27, 2020. https://professional.heart.org/professional/ScienceNews/UCM_505836_HFSAACCAH Astatement-addresses-concerns-re-using RAASantagonists-in-COVID-19.jsp
34. Hanff TC, Harhay MO, Brown TS, Cohen JB, Mohareb AM. Is There an Association Between COVID-19 Mortality and the Renin-Angiotensin System—a Call for Epidemiologic Investigations. Clin Infect Dis. 2020 Mar 26.

35. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China Intensive Care Med (2020) published online March 3.

36. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020 Feb 24.
Figures and tables

Figure 1: *thoracic computed tomography scans* (CT) in patients infected with COVID19, showing typical lung feature with ground glass opacities and bilateral pachty shadow, from minor (A) to severe pattern (D).
Figure 2: Lung ultrasound showing B line in a patient with COVID-19 infection
### Table 1. Studies about heart, ARDS and mortality in patients with COVID19

| N Patients | Critically ill patients / ICU admission | MV | Comorbidities or Chronic illness | ARDS | Cardiac Injury | Mortality in hospital | Mean age at inclusion | First author (ref) |
|------------|----------------------------------------|----|----------------------------------|------|----------------|-----------------------|----------------------|-------------------|
| 191        | 26% (ICU)                              | 17%| 48%                              | 31%  | 23% (HF)       | 28%                   | 56 y                 | Zhou (12)         |
| 52         | 100% (ICU)                             | 71%| 40%                              | 29%  | 29%            | 61% (at 28 days)      | 59.7 y               | Yang (13)         |
| 138        | 26% (ICU)                              | 23%| 72%                              | 19%  | 16.7% (arythmia) | 7.2% (ACI)            | 4.3%                 | Wang (3)          |
| 99         | 23% (ICU)                              | 17%| 51%                              | 17%  | 15% (myoglobin increase) | 11%                  | 55.5 y               | Chen (11)         |
| 41         | 32% (ICU)                              | 10%| 32%                              | 29%  | 12%            | 15%                   | 49 y                 | Huang (2)         |
| 21 (ICU)   | 100% (ICU)                             | 71%| 100%                             | 33%  | 67%            | 70 y                  |                      | Arentz (18)       |
| 24         | 100% (ICU)                             | 75%| 58% (diabetes) 21% (CKD)         | 15%  | 50%            | 64+-18 y              |                      | Bhatraju (21)     |
| 1099       | 5% (ICU)                               | 6.1%| 23.7%                           | 3.4% | 23.7% (increase CK) | 1.4%                 | 47 y                 | Guan (9)          |
| 416        | 20%                                    | 30.5% (HBP) 14.4% (diabetes) 10.6% (coronary disease) | 23.3% | 19.7% | 55.7% | 64 y | Shi (24) |
| 187        | 24.1%                                  | 32.6% (HBP) 11.2% (CHD) 15% (diabetes) | 24.6% | 27.8% | 23% | 58.7 y | Guo (10) |

ACI: acute cardiac injury; ARDS: acute respiratory disease syndrome; CK: creatine kinase; CKD: chronic kidney disease; CHD: coronary heart disease; HBP=high blood pressure; HF: heart failure; ICU: intensive care unit MV: mechanical ventilation; ref: number of reference; y: years
Table 2: Risk factors associated with mortality in patients with COVID-19 infection.

| Factors associated with mortality | OR or HR | N (patients) | First author (ref) |
|----------------------------------|----------|--------------|--------------------|
| Older age                        | 1.1 (OR) | N= 191       | Zou (12)           |
| Higher SOFA                      | 5.6 (OR) | N=416        | Shio (24)          |
| D-Dimers>1microg/ml              | 18.4 (OR)| N=1591       | Grasselli (22)     |
| Cardiac injury                   | 3.4 (HR) | N=416        |                    |
| ARDS                             | 7.11 (HR)| N=21         | Arentz (18)        |
| Age ≥64 years                    |          |              |                    |
| Age 70 years                     |          |              |                    |

HR: hazard ratio; N: number of patients; OR: odd ratio; SOFA: sequential organ failure assessment.