REVIEW

The impact of SARS-CoV-2 treatment on the cardiovascular system: an updated review

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Abstract

The coronavirus disease-2019 (COVID-19) pandemic has become a major global health problem. COVID-19 is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and exhibits pulmonary and extrapulmonary effects, including cardiovascular involvement. There are several attempts to identify drugs that could treat COVID-19. Moreover, many patients infected with COVID-19 have underlying diseases, particularly cardiovascular diseases. These patients are more likely to develop severe illnesses and would require optimized treatment strategies. The current study gathered information from various databases, including relevant studies, reviews, trials, or meta-analyses until April 2022 to identify the impact of SARS-CoV-2 treatment on the cardiovascular system. Studies have shown that the prognosis of patients with underlying cardiovascular disease is worsened by COVID-19, with some COVID-19 medications interfering with the cardiovascular system. The COVID-19 treatment strategy should consider many factors and parameters to avoid medication-induced cardiac injury, mainly in elderly patients. Therefore, this article provides a synthesis of evidence on the impact of different COVID-19 medications on the cardiovascular system and related disease conditions.

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Introduction

The World Health Organization (WHO) reported on March 12, 2020, that a new pneumonia-like disease caused by a coronavirus (COVID-19) has become a global pandemic due to its fast transmission, resulting in a substantial political and economic impact globally (World Health Organization 2020). The disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which belongs to a new type of beta-coronavirus characterized by its strong transmission and high pathogenicity (Lancet 2020). Most patients infected with SARS-CoV-2 virus who developed COVID-19 experience respiratory symptoms, manifested as fever, dry cough, and fatigue, accompanied by nasal congestion, runny nose, sore throat, muscle aches, and diarrhea. While some critically infected patients often develop acute respiratory distress and multiorgan failure (Wang et al. 2020a; Huang et al. 2020). Previous studies have shown that the prognosis of patients with underlying cardiovascular disease is worsened by COVID-19, with some patients having myocardial damage related to viral infection (Zhu et al. 2020). In addition, some studies have reported that patients infected with COVID-19 may have various cardiac manifestations, such as arrhythmia and cardiac arrest (Huang et al. 2020; Chen et al. 2020; Wang et al. 2020a; Marfella et al. 2021). Several medications, including antiviral drugs, are essential in managing COVID-19. Therefore, this article provides a synthesis of evidence on the impact of COVID-19 medications on the cardiovascular system and related disease conditions.

COVID-19 and the cardiovascular system

The coronavirus that causes COVID-19 is a positive, single-stranded RNA virus. Whole-genome sequence analysis of SARS-CoV-2 shows 79.6% homology to severe acute respiratory syndrome coronavirus (SARS-CoV) and the ST-elevations encoded by the two. The protein is similar to the angiotensin-converting enzyme 2 (ACE2) receptor domain (Zhou et al. 2020). Studies have shown that after entering the human body, COVID-19 enters cells primarily through ACE2 (Wang et al. 2020b), which in turn increases the level of angiotensin (AngII), leading to multiple organ dysfunctions, including cardiovascular diseases (Liu et al. 2020). Recent data shows that COVID-19 can be complicated by acute myocardial injury, mainly manifested by increased levels of highly sensitive myocardial injury markers of troponin I (cTnI) and creatine kinase isoenzyme (CK-MB) (Xu et al. 2020). In addition, the mean systolic blood pressure of critical patients with COVID-19 is higher than that of non-critical patients, and may be related to decreased expression of ACE2 and increased expression of AngII (Chen et al. 2020). Moreover, studies have shown that 16.7% of patients with COVID-19 have arrhythmia, mainly manifesting as fever-induced tachycardia (Chen et al. 2020). Although patients with COVID-19 suffer mainly from respiratory dysfunction, studies have shown a high proportion of up to 40% of the patients with cardiovascular disease come down with complications (Wang et al. 2020a), Fig. 1. Therefore, the pharmacological treatment of patients with COVID-19 and underlying cardiovascular disease deserves attention.

Fig. 1 Relationship between COVID-19 and the cardiovascular system
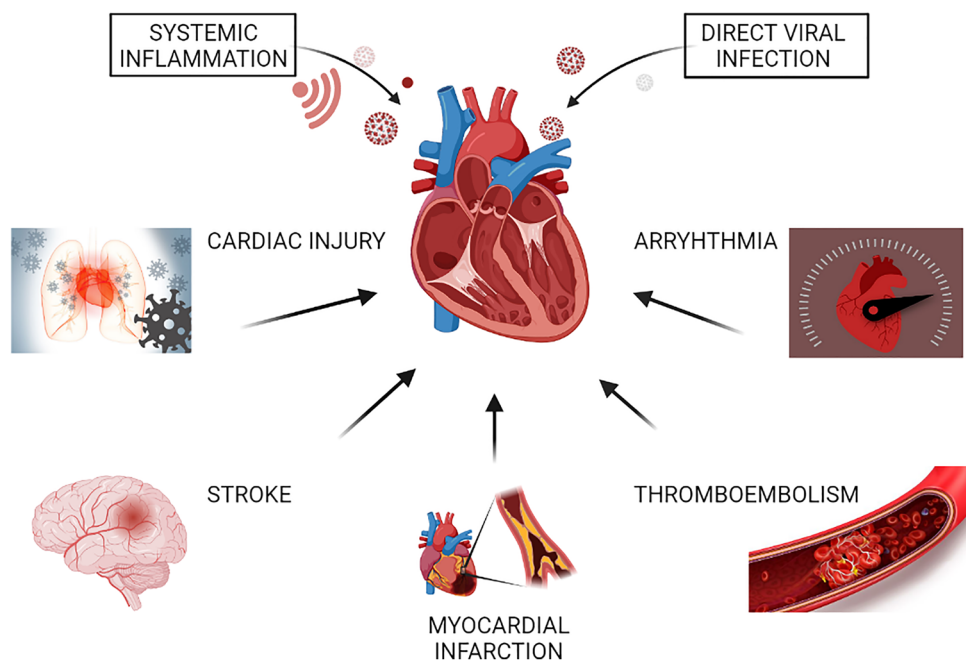
Therapeutic agents for COVID-19 and cardiovascular system

The accelerated spread of SARS-CoV-2 worldwide and the limited knowledge of its pathogenesis have led to the use of drugs, often empirically, without evidence of their actual efficacy for COVID-19. In addition to invasive or non-invasive ventilatory support, therapeutic choices have been directed toward antivirals and immunomodulators, either alone or in combination. These drugs were already known to treat other rheumatological, infectious and auto-immune diseases. Their use can affect the cardiovascular system, especially in patients with cardiovascular disease and coronary artery disease, either directly or through interaction with other drugs. The aim of this study is to explain the impact of antivirals and immunomodulators on the cardiovascular system, especially in a clinical setting, where cardiac damage may be an integral part of COVID-19.

Antiviral agents

Lopinavir/ritonavir (LR), a combination drug used to treat HIV, inhibits 3-chymotrypsin-like protease and papain-like protease in SARS-CoV-2, thereby blocking viral replication (Mody et al. 2021; Osipiuk et al. 2021). However, in a trial by Cao et al. (2020), the use of LR in adults hospitalized for SARS-CoV-2 infection did not result in any clinical benefit beyond standard care. LR, which belongs to the protease inhibitor group, increases the risk of coronary artery disease. The underlying mechanism is not yet clear, but it is partly due to the increase in total cholesterol and LDL-cholesterol, which underlies atherosclerotic disease (Friis-Møller et al. 2007; Fontas et al. 2004). In addition, Mondy et al. (2011) have shown that ritonavir can cause left ventricular dysfunction, dilation of the left atrium, and pulmonary hypertension through endothelial and pulmonary vascular muscle damage. Finally, LR combination therapy can cause a reversible prolongation of the PR interval, which is a limiting factor for its use (Ou et al. 2021).

Atazanavir is also a protease inhibitor that blocks SARS-CoV-2 replication in vitro, for which trials are ongoing to demonstrate efficacy in humans (Fintelman-Rodrigues et al. 2020). Atazanavir can cause PR and QT prolongation and a few cases of torsades de pointes, especially in the presence of congestive heart failure and electrolyte abnormalities (Soliman et al. 2011; Ly and Ruiz 2007). A study of patients with HIV showed that atazanavir reduced the risk of myocardial infarction and stroke compared with darunavir, which is partly explained by changes in serum bilirubin (Li et al. 2020).

Ribavirin is a guanosine analog antiviral approved for HCV and RSV. Currently available data have not shown improved outcomes in patients with COVID-19 (Tong et al. 2020). It has no direct effect on the cardiovascular system, but it can cause anemia and, consequently, myocardial ischemia (type 2 myocardial infarction), especially in patients with known coronary atherosclerosis (Macedo and Ribeiro 1999). An important pharmacokinetic feature of ribavirin is its ability to inhibit the activity of warfarin, which, therefore, requires a dose adjustment of the anticoagulant (Schulman 2002).

Ivermectin is not an antiviral but is an antiparasitic drug approved to treat scabies, strongyloidiasis, and trichuriasis. Although it has been demonstrated to block SARS-CoV-2 replication in-vitro, evidence in humans is lacking (Caly et al. 2020). It has no significant impact on the cardiovascular system, except for cases of hypotension and tachycardia without hemodynamic instability (Sparsa et al. 2006).

Remdesivir is an adenosine analog that inhibits viral RNA polymerase. It can shorten hospitalization times in patients admitted for COVID-19 (Beigel et al. 2020), but further studies are needed to confirm efficacy against SARS-CoV-2 infection. On its effects on the cardiovascular system, a study by Grein et al. (2020) revealed that hypotension was associated with remdesivir administration in patients with COVID-19 (4%) receiving invasive ventilation.

Immunomodulatory drugs

Hydroxychloroquine (HCQ) is widely used to treat malaria and some rheumatological diseases. It can block L-cathepsin activation in SARS-CoV-2, thereby interfering with endosomal acidification and preventing viral entry into the cell. However, despite initial encouraging data, no study has demonstrated the efficacy of HCQ against SARS-CoV-2 infection (Pastick et al. 2020). The cardiotoxicity of HCQ has been known for a long time. In acute cases, this may be due to its "quinidine-like" effects leading to a widened QRS interval and QT prolongation and increasing the risk of torsades de pointes. Other possible electrical complications include atrioventricular block, sick sinus syndrome, and right or left bundle–branch block.

Chronic toxicity results mainly in left ventricular hypertrophy, ventricular hypokinesia, and atrial dilatation. Very rare complications include pulmonary hypertension, valvular regurgitation, and restrictive cardiomyopathy. These effects are attributable to the intracellular accumulation of toxic metabolites, necrosis of cardiomyocytes and mitochondrial damage. Examination by electron microscopy has shown curvilinear bodies and lamellar structures due to

the accumulation of glycolipids and glycoproteins (Nadeem et al. 2021; Chen et al. 2006; Chatre et al. 2018).

Tocilizumab (TCZ) is an anti-interleukin-6 monoclonal antibody approved for the treatment of rheumatoid arthritis (Alten 2011). In patients with COVID-19, TCZ can counteract the inflammatory cascade. Nevertheless, in the COV-ACTA trial (Rosas et al. 2021), TCZ did not improve outcomes in SARS-CoV-2 infection compared with the placebo. Cacciapaglia's analysis of patients with rheumatoid arthritis demonstrated that treatment with TCZ is associated with an increase in cholesterol and all its fractions. The trend is "bell-shaped," indicating an increase in the first 6 months of treatment and then a return to baseline by month 12. Despite these changes, TCZ therapy does not increase cardiovascular risk (Cacciapaglia et al. 2018).

Finally, type-I interferons (IFN) are polypeptides involved in inflammation and immune response. Preliminary studies have demonstrated the efficacy of IFN in blocking SARS-CoV-2 replication, either alone or in combination with antiviral drugs (Hensley et al. 2004; Lokugamage et al. 2020). A trial is currently ongoing to determine the efficacy and safety of IFN-α2β in COVID-19 pneumonia (Zhao 2020). Teragawa et al. (1996) concluded that bradyarrhythmias, tachyarrhythmias, and ischemic heart disease frequently occur in patients with hepatitis C treated with IFN. The underlying mechanisms are still unclear, but IFN appears to cause coronary spasm, endothelial damage, increased oxygen demand, and immune-mediated myocardial damage.

Fingolimod is an immune modulator that blocks sphingosine-1-phosphate receptors, thereby interfering with the activation of B and T lymphocytes. It is currently used to treat multiple sclerosis (Chun and Brinkmann 2011), and studies are ongoing to assess its efficacy in patients with COVID-19 (NCT04280588).

Regarding cardiovascular risks, fingolimod may cause bradycardia, which is generally transient, well-tolerated, and rarely fatal (Singer et al. 2011). It confers an atheroprotective effect by reducing atherosclerotic plaque volume (Gräler and Goetzl 2004). Spasm of the retinal artery and retinal vein has been reported, probably due to the increased release of intracellular calcium (Enosawa et al. 1996; English et al. 2000). A similar effect on the systemic circulation causing arterial hypertension has also been observed (Behjati et al. 2014).

Azithromycin is a macrolide widely used in SARS-CoV-2 infection for its immunomodulatory activity. However, it has not demonstrated superiority in efficacy in patients with COVID-19 compared with the prevailing standard of care (Mangkuliguna et al. 2021). It can cause prolongation of the QT interval and, when used in combination with drugs that have the same effect, increases the risk of lethal arrhythmias, such as torsades de pointes (Hancox et al. 2013).

Corticosteroids (CS) are potent anti-inflammatory drugs that can improve outcomes in patients hospitalized for COVID-19. Several studies have shown that they reduce disease progression and mortality rates and increase ventilator-free days (Crisan Dabija et al. 2021). On its cardiovascular effects, CS can cause arterial hypertension by stimulating the renin–angiotensin–aldosterone system, excessive sodium retention, and catecholamine synthesis. Prolonged CS therapy can cause hyperglycemia and hyperlipidemia, thus increasing the cardiovascular risk (Sholter and Armstrong 2000).

Combined treatment of COVID-19 and cardiovascular complications

A meta-analysis has shown the association between COVID-19 infection and the tendency to develop viral myocarditis and abnormal cardiac biomarkers, including troponin I and creatinine kinase (Lippi et al. 2020). This association explains why the reported mortality rates are higher in COVID-19 patients with pre-existing cardiovascular diseases (Talasaz et al. 2020). Apart from the SARS-CoV-2 virus, which is accountable for causing the COVID-19 disease, the drug–drug interactions that may arise in COVID-19 patients with pre-existing cardiovascular conditions such as heart failure, arrhythmias, and acute ischemic stroke coronary syndrome (ACS) may also complicate the prognosis of the infectious disease (Talasaz et al. 2020). This section of the current review will discuss the drug–drug interactions of concern in COVID-19 patients based on the different types of pre-existing cardiovascular diseases (Dinan et al. 2015).

Heart failure

Considering the possible drug–drug interactions in heart failure patients who acquired COVID-19 infection. Angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), angiotensin receptor–neprilysin inhibitor (ARNI), β-blockers, ivabradine, digoxin, diuretics, nitrates are among the commonly used drugs in the treatment of acute and chronic heart failure (Talasaz et al. 2020; McMurray et al. 2012). Most of these drugs have clinically significant interactions with certain medications used to manage COVID-19 (Giguère et al. 2019; Dixon et al. 2020).

Lopinavir/ritonavir from the class of protease inhibitors is considered among the promising drugs in managing COVID-19. However, clinical trials to finalize the efficacy of these drugs in managing COVID-19 are still ongoing (Meini et al. 2020). In COVID-19 patients on lopinavir/ritonavir receiving β-blockers, diligent blood pressure and heart rate monitoring is greatly recommended (Talasaz et al. 2020). This is because ritonavir has been reported to affect the metabolism of certain β-blockers, such as bisoprolol, carvedilol, and metoprolol (Giguère et al. 2019). However,

the interaction between lopinavir/ritonavir and bisoprolol is of weak intensity, and these drugs can be administered concurrently with appropriate monitoring.

Meanwhile, concurrent administration of metoprolol or carvedilol with lopinavir/ritonavir was reported to increase the blood levels of these two β-blockers to a moderate extent (Agarwal and Agarwal 2020). Hydroxychloroquine is an antimalarial drug that was earlier used to manage COVID-19 (Singh et al. 2020). This drug may cause bradycardia, which may be worsened by the concomitant use of β-blockers in COVID-19 patients. Meticulous blood pressure and heart rate monitoring are required in COVID-19 patients receiving any β-blockers (Talasaz et al. 2020). However, it should be noted that a recent Cochrane review reports that the use of this antimalarial agent is less likely to be effective in the management of COVID-19 (Singh et al. 2020).

In the class of ARNI, sacubitril's plasma concentration increases the following coadministration with ritonavir, which warrants close surveillance of serum potassium level, serum creatinine level, and blood pressure (Talasaz et al. 2020). However, this interaction is considered quite controversial as some claim such interaction is unlikely (Hanna et al. 2018). More extensive studies are needed to verify the likelihood of the interaction between sacubitril and ritonavir.

Eplerenone is a mineralocorticoid receptor antagonist classified as a diuretic (Reyes et al. 2005). Concurrently administration of eplerenone with protease inhibitors may cause a fourfold hike in the area under the curve (AUC) of eplerenone, which translates into the delayed clearance of the drug from the body (Talasaz et al. 2020). Delayed clearance of eplerenone due to the said interaction leads to an increased risk of side effects, primarily hyperkalemia (Cordova et al. 2021). Alternatively, the use of spironolactone is recommended in COVID-19 patients on protease inhibitors. Another diuretic that has documented interaction with lopinavir/ritonavir is indapamide. However, this interaction cannot be concluded as a class effect as no drug–drug interaction is known to exist between lopinavir/ritonavir and thiazide diuretics, generally (Talasaz et al. 2020). CYP3A4 enzyme is an extensive metabolizer of indapamide (Sun et al. 2009). Coadministration of indapamide with lopinavir/ritonavir increases the serum concentration of the former. This is due to the nature of lopinavir/ritonavir, which inhibits the CYP3A4 enzyme (Agarwal and Agarwal 2020). Great caution is needed with the concomitant use of indapamide with lopinavir/ritonavir (Talasaz et al. 2020). To minimize the undesirable effects of such interactions, it is recommended to reduce the indapamide dose (Agarwal and Agarwal 2020).

Patients hospitalized for COVID-19, while on digoxin treatment require close monitoring, since there are chances of instability during acute infection. The therapeutic drug monitoring for digoxin is essential due to the changes in its serum concentration when used concomitantly with some drugs used in the treatment of COVID-19, such as ritonavir and hydroxychloroquine. Hydroxychloroquine may increase the serum digoxin concentration via an unknown mechanism. Meanwhile, ritonavir may increase the half-life of digoxin by 43% and may increase the AUC of digoxin by 29% (Dixon et al. 2020). Another study in healthy volunteers reported increased digoxin plasma concentrations when given concomitantly with ritonavir (Penzak et al. 2004). Before initiating lopinavir/ritonavir, it is recommended to reduce the dose of digoxin given to a patient by 50%. Such reduction should be followed by extensive monitoring of the patient's serum digoxin levels, ECG, and clinical signs and symptoms relevant to the indication of digoxin (Agarwal and Agarwal 2020).

The clinically significant interaction between hydralazine and protease inhibitor is less likely (Giguère et al. 2019; Agarwal and Agarwal 2020). However, COVID-19 patients on concomitant administration of hydralazine or nitrates and protease inhibitors are entitled to dosage adjustments based on their drug response (Talasaz et al. 2020).

The formation of nitric oxide from isosorbide dinitrate can be diminished following the coadministration of protease inhibitors. CYP3A4 enzyme, which mediates the biotransformation of nitric oxide, will be inhibited by lopinavir/ritonavir when administered concurrently. Such inhibition of CYP3A4 eventually leads to reduced efficacy of isosorbide dinitrate. However, the clinical relevance of this drug–drug interaction is yet to be established, and monitoring is recommended (Agarwal and Agarwal 2020; Giguère et al. 2019).

The use of ivabradine should ideally be avoided in COVID-19 patients on lopinavir/ritonavir, as the incidence of severe symptomatic bradycardia is likely (Dixon et al. 2020; Romero-León et al. 2016). Lopinavir/ritonavir are potent inhibitors of the CYP3A4 enzyme, which happens to be the metabolizer of ivabradine (Dixon et al. 2020; Chaudhary et al. 2016). Concurrent administration of lopinavir/ritonavir can increase the area under the curve (AUC) of ivabradine by sixfold, which in turn increases the toxicity of ivabradine (Dixon et al. 2020).

Arrhythmia

According to a study conducted in Wuhan, COVID-19 infection itself was found to cause arrhythmia in 44% of patients (Alhazzani et al., 2021). Thus, extra attention is warranted in COVID-19 patients with pre-existing arrhythmia. Possible drugs that may precipitate arrhythmia in COVID-19 patients should be used with caution or avoided. In COVID-19 patients with shock, the use of dopamine as a vasopressor should be avoided as it increases the risk of arrhythmias and mortality. However, the recommendation is derived from clinical trials conducted among critically ill patients, not COVID-19 patients with shock. Thus, more research should

be done to conclude the direct of dobutamine on COVID-19 patients with shock (Alhazzani et al. 2021).

In COVID-19 patients, the QTc prolongation risk and torsade de Pointes (TdP) risk are elevated with the simultaneous use of antiarrhythmic agents and chloroquine/hydroxychloroquine. ECG monitoring should be performed before the treatment initiation to manage such risks appropriately. Moreover, it is also essential to maintain the serum potassium level above 4.5 mg/dL and serum magnesium level above 2 mg/dL as a part of the ideal monitoring parameters for the said risks (Baigent et al. 2022; Zeitlinger et al. 2020).

COVID-19 treatment regimens that incorporate the simultaneous use of chloroquine/hydroxychloroquine and lopinavir/ritonavir should be avoided. This is because such coadministration of the drugs may lengthen the QTc interval, which eventually increases the tendency to develop TdP (Zeitlinger et al. 2020; Giudicessi et al. 2020). Moreover, concomitant usage of these drugs is attributed to the atrioventricular block risk. Few forms of alterations in the cardiac function are evident with chloroquine/hydroxychloroquine, which includes ventricular fibrillation, bundle branch block, and ventricular tachycardia (Driggin et al. 2020). The tendency for the incidence of drug-induced sudden cardiac death is increased with the combination of chloroquine/hydroxychloroquine and lopinavir/ritonavir, which is QTc prolonging drugs on their own (Giudicessi et al. 2020).

The effects of antiarrhythmic drugs such as amiodarone, quinidine, and lidocaine can be affected by concurrent administration of protease inhibitors in COVID-19 patients with pre-existing arrhythmia. Thus, ECG surveillance is essential in patients on both drugs, and in some instances, dose reduction may also be considered. If quinidine or lidocaine is used along with amiodarone, regular monitoring of thyroid function, liver function, and blood pressure should be instituted. Concurrent administration of flecainide, a class 1c antiarrhythmic and protease inhibitor, such as ritonavir, is contraindicated (Zeitlinger et al. 2020).

Acute Coronary Syndrome

In the presence of ACS, antiplatelets, anticoagulants, thrombolytics, HMG-CoA reductase inhibitors, β-blockers, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) are among the commonly used drugs (Talasaz et al. 2020).

In COVID-19 patients with ACS, a drug interaction is likely between ARBs and lopinavir/ritonavir. Losartan and irbesartan may lose their efficacy when used concurrently with ritonavir. Such loss in effectiveness is attributed to the diminished ability of the said ARBs to transform into their active forms, in which their efficacy is optimal (Giguère et al. 2019). COVID-19 patients on ACEIs or ARBs should be closely monitored for their serum potassium level, serum creatinine level, and blood pressure (Dixon et al. 2020).

Another significant drug–drug interaction that should be considered in COVID-19 patients with ACS is the interaction between P2Y12 inhibitors and protease inhibitors. In COVID-19 patients receiving lopinavir/ritonavir, the use of ticagrelor is contraindicated. Lopinavir/ritonavir may also decrease the antiplatelet property of clopidogrel; thus, dosing adjustment for clopidogrel is recommended. Prasugrel is named a better alternative, which can be concurrently administered along with lopinavir/ritonavir in patients without risk of bleeding and coagulopathy (Bikdeli et al. 2020). The use of glycoprotein IIb/IIIa inhibitors should be avoided due to the high tendency to develop acute kidney injury and increased risk of bleeding in COVID-19 patients. Considering the increased risk for the incidence of thrombocytopenia, the use of abciximab should ideally be avoided. Instead, they use eptifibatide, and tirofiban can be regarded when required (Ibanez et al. 2018).

Upon hospitalization, switching to parenteral anticoagulant is preferred in COVID-19 patients on chronic treatment with anticoagulants (Bikdeli et al. 2020). Regarding drug–drug interaction, the use of warfarin and drugs used for COVID-19 is not contraindicated, given that monitoring of the international normalized ratio (INR) is performed periodically. In the context of anticoagulants, apixaban and rivaroxaban have lesser interactions with chloroquine/hydroxychloroquine as compared to edoxaban and dabigatran. However, due to the elevated tendency of bleeding, the simultaneous use of lopinavir/ritonavir and rivaroxaban is contraindicated (Baigent et al. 2022). The administration of edoxaban with lopinavir/ritonavir is not well studied; thus, it is not recommended. The dose of apixaban is recommended to be reduced by half when administering concomitantly with lopinavir/ritonavir. Meanwhile, dabigatran can be given at a conventional dose with a 2-h dosing interval with lopinavir/ritonavir (Dixon et al. 2020; Baigent et al. 2022; Wiggins et al. 2020).

Lopinavir/ritonavir has a likely interaction with rosuvastatin and atorvastatin. Rosuvastatin and atorvastatin belong to the group of HMG–CoA reductase inhibitors. Concerning this drug–drug interaction, it is recommended that the maximum daily dose of rosuvastatin and atorvastatin should be capped at 10 mg and 20 mg, respectively, when used concomitantly with lopinavir/ritonavir (Newman et al. 2019). When used concurrently, tocilizumab may decrease the serum concentrations of the HMG–CoA reductase inhibitors. This is due to the reversal of cytochrome P450 (CYP450) suppression resulting from tocilizumab. The clinical impact of this interaction can be diminished by the short-term use of anti-interleukin-6 receptor treatments (Dixon et al. 2020).

Conclusions

The therapeutic management of COVID-19 should consider cardiovascular disease involvement and adapt the most beneficial and optimized treatment plan. The treatment strategy should consider patient's cardiovascular indices; heart rate, blood pressure, blood lipids, heart function, and ECG changes. To avoid medication-induced cardiac injury, it is important to pay attention to drug interactions. Simultaneously, the monitoring of important signs for the identification of myocardial damage should be bolstered, and the heart function of COVID-19 patients should be assessed using laboratory and imaging data. Currently, the recommendations do not suggest using more than three antiviral medications in combination, and caution should be exercised in elderly patients with COVID-19 and underlying cardiovascular illnesses.

Declarations

Ethics approval and consent to participate. Not applicable.

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