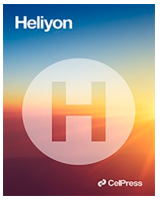
Heliyon 10 (2024) e39345

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Review article

Perioperative cardiovascular risk and preventions of patients with post-COVID-19 condition

Sixu Lai , Su Min *

Department of Anesthesiology, The First Affiliated Hospital of Chongqing Medical University, China

ARTICLE INFO

Keywords:
COVID-19
Cardiovascular system
Perioperative period
Post-COVID-19 condition

ABSTRACT

COVID-19 infectious is still a widely prevalent disease today. Although most patients with COVID-19 infection are mild. Some patients still develop to post-COVID-19 conditions, significantly increasing the perioperative cardiovascular risks. To better assess and prevent the perioperative cardiovascular risks of patients with COVID-19 infection, the safety and effectiveness of clinical practice can be improved through comprehensive measures, such as medical history collection, detection of symptoms and signs, application of auxiliary examinations, selection of scales and related rehabilitation treatment.

1. Introduction

Data show that [1]more than 700 million people have been infected with the COVID-19 worldwide, with 99.8 % of patients being mild and 0.2 % severe [1]. Although the symptoms of most COVID-19 patients can disappear within a few weeks, it is estimated that long-term COVID-19 infection occurs in 10–20 % of cases and affects people of all ages, which is a huge challenge for the current medical environment [2] (see Fig. 1)

In 2022, the WHO defined "post-COVID-19 condition" as symptoms that occur within 3 months of confirmed or suspected COVID-19 infection, persist for at least 2 months and cannot be explained by other diagnoses [3]. Studies have reported that COVID-19 infection significantly increases the risk of stroke, arrhythmia, and other cardiovascular complications during surgery, leading to higher mortality rates [4–7]. These risks are associated with acute severe infection, as well as age, race, gender, and other cardiovascular risk factors such as obesity, hypertension, diabetes mellitus, chronic kidney disease, and hyperlipidemia [4,5,8,9]. Doctors should prioritize exploring perioperative cardiovascular risks and precautions. This literature review will summarize and discuss perioperative cardiovascular risks, preventive measures, and future directions for patients with post-COVID-19 condition.

2. Mechanism of cardiovascular damage caused by COVID-19 infection

2.1. SARS-COV-2 directly invades and damages the cardiovascular system?

The prevailing view is that the receptor of host cells is a key factor in the damage caused by COVID-19 infection. ACE-2 is considered to be the main "gateway" for COVID-19 invasion [10]. In the cardiovascular system, ACE-2 is distributed widely, including cardiomyocytes, endothelial cells, fibroblasts, and smooth muscle cells [11]. SARS-COV-2 binds to ACE-2 through the spike protein on

* Corresponding author.
E-mail address: ms89011068@163.com (S. Min).

https://doi.org/10.1016/j.heliyon.2024.e39345
Received 28 April 2024; Received in revised form 9 October 2024; Accepted 11 October 2024
Available online 15 October 2024

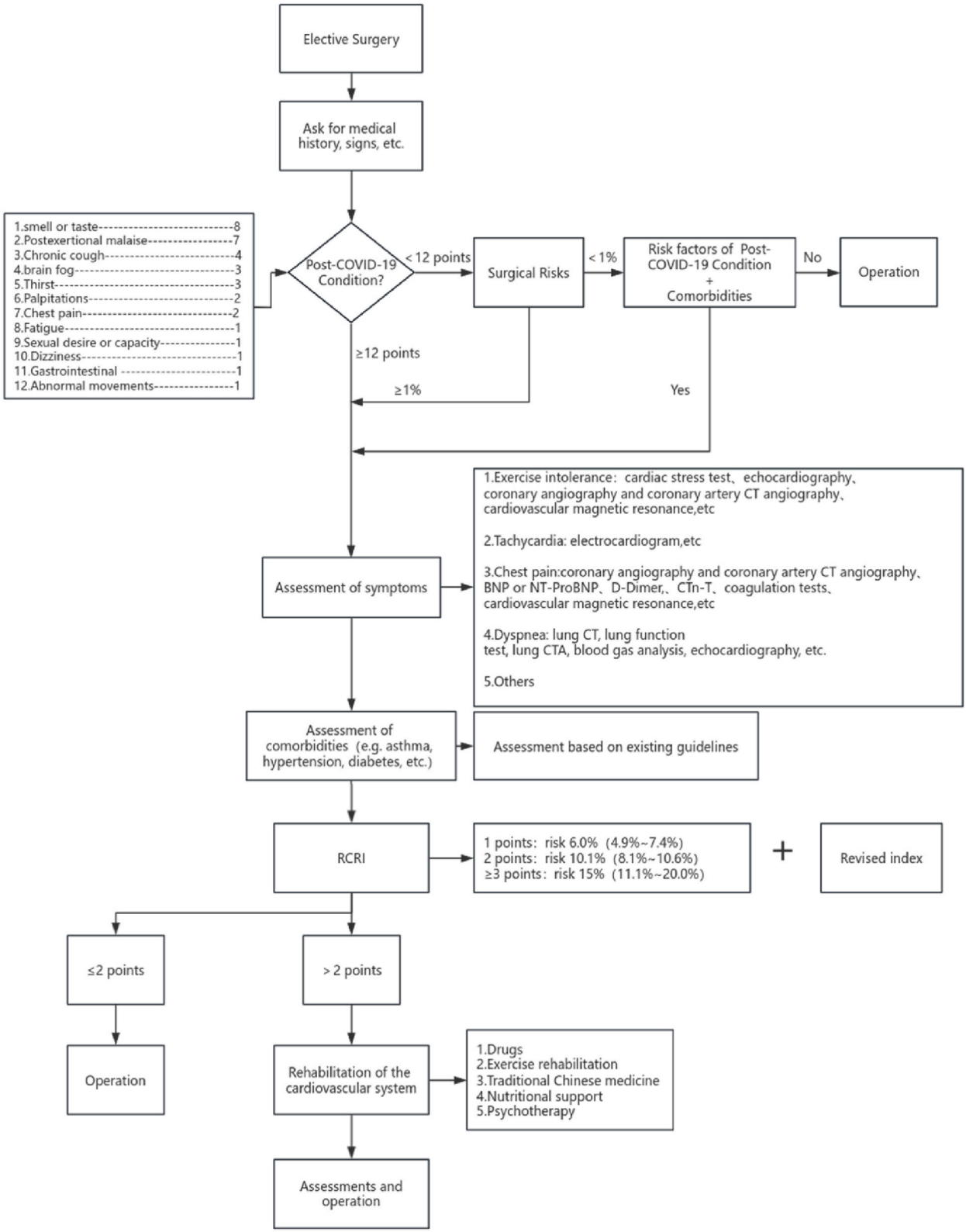


Fig. 1. Perioperative cardiovascular risk assessment process in patients with post-COVID-19 condition.
* Note: 1. Revised index (1 point per item): patient self-reported activity tolerance less than 4 METS, coronary CTA suggesting calcification score 113 points and (or) any coronary stenosis 50 % and (or) more coronary abnormalities [52].

the surface, promotes the fusion of the virus and then increases the viral load through replication and transcription, which leads to the cell lysis and apoptosis of the cardiovascular system, and causes direct damage to the cardiovascular system [12,13]. On further investigation, the researchers found that receptors such as ASGR1, KREMEN1, TMEM106B and neuropilin-1 may also mediate the interaction between SARS-COV-2 and the host [14,15].

However, some researchers have failed to find the SARS-COV-2 inclusion body in the myocardial autopsy results of COVID-19 infected patients [16]. Positive rate of cardiac COVID-19 nucleic acid test is also very low. The autopsy evidence presented does not support the notion that COVID-19 directly targets the cardiovascular system. Further studies are required to elucidate the precise mechanism of injury.

2.2. Inflammation and cytokine storm resulting from COVID-19 infection can damage the cardiovascular system

COVID-19 has the potential to cause damage to the cardiovascular system through excessive inflammation and cytokine storm. A study based on RNA-RNA interaction showed that SARS-CoV-2 may induce cardiovascular damage by stabilizing NFKBIZ, a kind of mRNA targets, to inhibit host cells and promote the production of more cytokines such as IL 6 and IL 8 [17]. Another study by examining coronary autopsy specimens from eight patients with COVID-19 infection found that COVID-19 could indeed infect and replicate in macrophages and foam cells in the coronary vessels of patients, triggering excessive inflammatory response by inhibiting the levels of type I interferon and maintaining the long-term infection status of SARS-CoV-2 [18]. Even more, severe COVID-19 infection can cause persistent changes in the innate immune phenotype and epigenetic program of hematopoietic stem cells and progenitor cells. These changes can cause organ dysfunction and inflammation, which can be inherited by subsequent cells [19].

2.3. Cardiovascular damage May result from the combined effects of multiple systemic organs

ACE-2 is also present in multiple systems, including the lung, gastrointestinal tract, and kidney [11]. However, the multiple organ damage caused by COVID-19 infection cannot be fully explained by the widespread presence of ACE-2 alone. Through the analysis of the SARS-COV -2 spike protein, researchers found several protein pathways of virus entry, immune regulation, Wnt pathway and protein transport [15], which further explains the mechanism of COVID-19 infection and multiple organ damage. An imaging report on multiple organs in patients with COVID-19 infection revealed that after 5 months of infection, over 30 % of patients had more than one organ abnormality [20]. After 6 months of infection, over 60 % of patients had multi-organ function damage, with the most severe injuries occurring in the head and lungs [20]. The studies above show that “long-term COVID-19” is not caused by serious defects in one organ, but rather is a common result of multiple system abnormalities. However, the evidence for the internal association of COVID-19 patients with multi-system abnormalities is still insufficient and requires further investigation.

3. Cardiovascular risks during the perioperative period in patients with post-COVID-19 condition

3.1. Stroke

The incidence of stroke in COVID-19 patients was 1.53 times higher than in uninfected patients, with ischemic stroke and transient ischemic attacks (TIA) being the most common types [5]. This may be due to immune-mediated platelet activation, which accelerates thrombosis. Additionally, depletion of ACE-2 leads to elevated angiotensin II, promoting inflammation and the release of cytokines, activating the coagulation pathway and producing thrombin [21].

3.2. Arrhythmia

The incidence of arrhythmia during non-cardiac surgery in COVID-19 patients was found to be 24 % [22], with the most common types of arrhythmia observed being sinus tachycardia [5] and atrial fibrillation [8]. A study utilizing the Swedish national database demonstrated that COVID-19 is an independent risk factor for arrhythmia, particularly in severe cases, unvaccinated individuals, the elderly, and those with underlying health conditions [23].

3.3. Inflammatory heart disease

Patients with post-COVID-19 condition exhibited high levels of cardiac inflammation, regardless of the severity of the infection [24]. A proteomics-based study revealed that COVID-19 infection significantly upregulates inflammation-related proteins and downregulates energy metabolism and heart conduction-related proteins [25]. Although the virus itself affects the heart and microvessels, it appears to have less effect on heart function changes. Cardiovascular system dysfunction is more likely to be driven by the virus of inflammation [25].

3.4. Ischemic cardiomyopathy

Patients with post-COVID-19 condition are at a 1.7-fold increased risk of perioperative ischemic cardiomyopathy [5]. The pathogenesis may be related to inflammation, thrombosis, and endothelial cell damage. Cytokine storm and a prothrombotic state can lead to atherosclerotic plaque instability and myocardial infarction. However, some studies suggest that COVID-19 may cause ischaemic

cardiomyopathy in the short term due to endothelial cell injury and dysfunction induced by the massive release of inflammatory factors and cytokines, leading to ischaemic injury of the non-vascular embolic type [26–28].

3.5. Thrombosis

A study revealed that patients who had contracted COVID-19 had a 22-fold higher risk of thrombosis within one year of recovery [8]. Previous studies have highlighted the thrombogenic roles of RAAS dysregulation and the microvascular immune response [27,29]. RAAS dysregulation promotes increased Ang II, reactive oxygen species, and endothelial dysfunction [30]. The immune response promotes thrombosis through the complement, NET, and MAPKS pathways. These factors combine to result in an impaired supply/demand balance of antifibrinolytic enzymes [29,31].

3.6. Others

In addition to the above risks, COVID-19 infection also significantly increases the perioperative risk of heart failure, cardiogenic shock, and cardiac arrest [5]. Although the incidence rate is very low, it is still important to pay attention to prevention and identification.

4. Revised cardiac risk index (RCRI)

The RCRI is relatively simple to use and includes the following main components: ischemic heart disease, cerebrovascular disease, heart failure, diabetes mellitus requiring insulin therapy, chronic kidney disease (serum creatinine level >2.0 mg/dL), and high-risk surgeries, each of which is worth a score of 1 point [32]. Studies indicats that adding patient self-report functional evaluation and combining coronary CTA to the evaluation tool can more accurately correct the perioperative risk classification of patients [33].

5. Preventive measures for perioperative cardiovascular risk in patients with post-COVID-19 condition

5.1. Medical history

When assessing patients for COVID-19 infection, it is important to gather their medical history. For patients suspected of experiencing sequelae of COVID-19, it is necessary to determine if they have any high-risk factors for 'long-term COVID-19′, such as being female, older age, obesity, asthma, poor general health, or poor previous mental health [34]. In addition, the medical history should identify any cardiovascular disease associated with major perioperative cardiovascular adverse events, including a history of ischemic heart disease, coronary stent implantation, heart failure, arrhythmia, valvular disease, hypertension, pulmonary hypertension, and risk factors for cardiovascular disease.

Furthermore, impaired exercise tolerance is a crucial factor in predicting perioperative cardiovascular risk. Previous study revealed that patient self-reported exercise tolerance is independently associated with the prediction of perioperative risk. Poor self-reported exercise tolerance is linked to more perioperative complications and a significant increase in cardiovascular complications [35]. When collecting a patient's medical history, it is recommended to inquire about their self-reported exercise tolerance. Typically, an assessment of 4 metabolic equivalents or above is selected. It is advised to ask if the patient can climb two consecutive floors, which is equivalent to 4 metabolic equivalents [33,35,36].

5.2. Symptoms

The reports indicate that between 9 % and 45 % of patients who have contracted COVID-19 continue to exhibit symptoms within a year after infection [37,38]. Even up to 31 % of patients still have long-term effects two years after infection [39]. Therefore, a study proposed a diagnostic tool for "long-term COVID-19″ based on symptoms, which summarized the sequelae of COVID-19 in the following 12 aspects: loss of or change in smell or taste, postexertional malaise(PEM), chronic cough, brain fog, thirst, palpitations, chest pain, fatigue, changes in sexual desire or capacity, dizziness, gastrointestinal symptoms, and abnormal movements [40]. Individuals with a total score greater than 12 are considered positive for post-COVID-19 condition. Symptom values are assigned to make this determination [40]. long-term COVID-19 is a diverse disease, encompassing a variety of cardiovascular symptoms. For instance, PEM and palpitations are the most prevalent, followed by chest pain and dyspnea [41]. However, when assessing patients, it is also important to exclude any preexisting cardiovascular symptoms or diseases.

5.3. Type of surgery

The type of surgery is strongly associated with the cardiovascular risk in the perioperative period. Based on the risk level of major cardiovascular adverse events or death, the European Heart Association (ESC) classifies the types of surgery as follows: (1) low-risk surgery (<1 %): ophthalmic surgery, breast surgery, short orthopedic surgery, etc.(2) Medium-risk surgery (1 %–5 %): orthopedic surgery, neurosurgery, peripheral vascular surgery, etc. (4) High-risk surgery (>5 %): adrenalectomy, aortic and macrovascular surgery, liver resection, pneumonectomy, etc [42].

5.4. Auxiliary inspection

5.4.1. Cardiac stress test

Studies have shown that patients with long-term COVID-19 are prone to fatigue, exercise intolerance and other symtoms [43], suggesting that there may be a decrease in cardiac reserve function. And the reserve capacity of the heart is closely related to the perioperative cardiovascular risk [35]. In clinical practice, the exercise cardiac stress test is the preferred method for evaluating cardiac reserve capacity. If the patient is unable to complete the exercise test, a drug cardiac stress test may be performed [44]. Cardiac stress test is recommended for patients with high cardiovascular risk index (RCRI score$\geq$ 2), poor self-reported exercise tolerance (<4 METs), or high-risk surgery with unknown cardiac reserve [45].

5.4.2. Electrocardiogram

COVID-19 infection may negatively affect the cardiovascular system and result in abnormal ECG readings. Long-term COVID-19 patients frequently exhibit sinus tachycardia [46]. Studies have revealed that the occurrence of any arrhythmia in patients with COVID-19 is associated with higher mortality as well as cardiovascular risk, where ST segment changes and tachycardia are independent predictors of adverse cardiovascular events [47,48]. Therefore, in patients with clinical symptoms, comorbid cardiovascular disease, the presence of high-risk factors, or those undergoing high-risk procedures, we recommend the routine use of electrocardiogram for preoperative evaluation.

5.4.3. Echocardiography

Approximately 70 % of COVID-19 patients exhibit echocardiographic abnormalities, with a predominance of left ventricular diastolic function and right ventricular dysfunction [49]. However, only 10 % have relevant symptoms even in critically ill patients [50].

5.4.4. Coronary angiography and coronary CT angiography

Numerous researches have found that patients with post-COVID-19 condition have a significantly increased risk of thrombosis and atherosclerosis [27,29,50]. Coronary CTA as a non-invasive technique has a negative predictive value of 96 % for the perioperative absence of cardiovascular adverse events [51]. If RCRI and coronary CTA are combined to evaluate the perioperative cardiovascular events, the value of RCRI will be amazingly improved [52]. Although coronary CTA may inappropriately overestimate the risk [53]. There is a possibility of perioperative coronary artery disease in patients with COVID-19 infections, further refinement of coronary CTA and, if necessary, coronary angiography is still recommended preoperatively.

5.4.5. Cardiovascular magnetic resonance(CMR)

CMR can provide valuable clues to the etiology of symptoms. The CMR can provide a noninvasive biopsy-like approach to validate the characteristic imaging features of myocardial inflammation [54]. Some studies have made the clinical diagnosis of myocarditis in 30 % of long-term COVID-19 patients through CMR [55]. And multiple organ dysfunction was found in patients with COVID-19 infection was highly sensitive [20]. Also CMR should also be considered in patients with suspected myocarditis after receiving the COVID-19 vaccine.

5.4.6. Measurement of the biomarkers

A meta-analysis showed that D-Dimer, CRP, LDH, leukocytes, lymphocytes, and IL-6 were remarkably increased compared with asymptomatic recovered patients. In the subgroup analysis, D-Dimer, LDH, and lymphocytes were significantly increased in patients with organ abnormalities. Only D-Dimer differed significantly over time [56].

In addition, BNP or NT-ProBNP were abnormal in 7 % of patients in the first 5 months after COVID-19 infection [50,56]. In the recovery period of COVID-19, higher CTn-T levels indicate more myocardial damage and myocardial scar, and myocardial scar is an independent predictor of cardiovascular risk in patients with long-term COVID-19 [57]. Researchers found that the circulating levels of BNP, CTn-T, CPR and D-Dimer were significantly increased in patients who died when compared with survivors [58]. Therefore, for patients with post-COVID-19 condition, cardiovascular risk factors and high-risk surgery, perioperative monitoring of BNP, NT-ProBNP and CTn-T changes is conducive to judging the myocardial injury progression and outcome of long-term COVID-19 patients, and is more conducive to risk stratification.

In addition, the extracellular matrix (ECM), perivascular fat attenuation index, glycated hemoglobin, serum lipids, and procalcitonin all contribute to the identification of risk factors and risk assessment [22,25,59–61]. However, the biomarkers in the current study lack predictivity of the existence and prognosis of long-term COVID-19.While metabolic phenotype studies have been used to identify new predictive markers of long-term COVID-19, they are still in the exploratory stage [62].

5.5. Rehabilitation of the cardiovascular system

5.5.1. Drugs

5.5.1.1. Beta-blockers. The available evidence shows that preoperative Beta-blockers administration can reduce the preoperative heart rate and improve the performance of tachycardia such as palpitations [63,64]. However, high-dose extended-release metoprollol

succinate (100 mg/d) starting immediately (<1 week) before surgery was significantly associated with increased perioperative stroke and mortality in patients with post-COVID-19 condition [32,63].

5.5.1.2. Statin drugs. Previous study has reported that statin use during surgical hospitalization is associated with reduced cardiovascular risk. However, a randomized trial of 80 mg of atorvastatin versus placebo within 18 h before surgery showed no significant benefit [65]. Prophylactic use should preferably be started more than 2 weeks before surgery to achieve the cumulative dose of protection [66]. Stains should be considered before surgery in patients with atherosclerotic cardiovascular disease, and are also recommended in surgical patients with high clinical risk [32].

5.5.1.3. Antiplatelet agents. Despite early patients with COVID-19 infection, selective COX-2 inhibitors such as celecoxib are recommended [67]. It can slow down the progression of COVID-19 infection and reduce the cost during hospitalization. However, the routine application of antiplatelet therapy before and during non-cardiac surgery is not recommended, because this has no more benefit and increases the risk of bleeding [32].

5.5.1.4. Anticoagulants. Patients with post-COVID-19 condition and coagulopathy may benefit from a continuous anticoagulant therapy regimen to regulate the supporting fibrinolytic system function [68]. Some researchers believe that anticoagulation therapy is the core of the comprehensive treatment of COVID-19 [69] with no anticoagulation for low-risk patients, prophylactic doses of anticoagulation for intermediate-risk patients, and therapeutic doses of anticoagulation for high-risk patients [30]. Our goal of anticoagulation therapy is not only to prevent thrombosis, but also to delay the development of multiple organ damage.

5.5.1.5. Angiotensin-converting enzyme inhibitor (ACEI) and angiotensin receptor blockers (ARB). It has been found that there was no significant difference in postoperative mortality and complications of ACEI or ARB in patients with COVID-19 infection [70]. However, the use of ACEI/ARB to rebalance the RASS system may alleviate the excessive inflammation and procoagulant state experienced by patients with long-term COVID-19 [71]. There is insufficient evidence to support modification or discontinuation of ACEI/ARBs in patients with COVID-19. However, ACEI/ARBs remain essential medications for patients with underlying cardiovascular disease.

5.5.1.6. COVID-19 vaccines. The most effective way to prevent long-term COVID-19 symptoms is to prevent infection in the first place, and vaccination is the best way [5]. At present, COVID-19 vaccines can be roughly divided into four categories: inactivated virus vaccine, protein subunit vaccine, viral vector vaccine and mRNA vaccine. Vaccination may improve the pathophysiological changes in patients with long-term COVID-19 [72], accelerating viral clearance and attenuating the chronic inflammatory response [73]. However,it is important to note that the post-COVID-19 condition cannot be completely eliminated [4].

In addition, some studies have found a possible association between acute pericarditis and COVID-19 vaccination [74]. The risk of pericarditis appears to be increased within the first week after vaccination, especially after the second dose, and is more commonly seen in younger males. But this risk is significantly lower than the risk associated with COVID-19 infection itself [75]. Research indicates that increasing the time interval between mRNA vaccine doses may decrease the risk of vaccine-induced myocarditis.

Moreover, recent reports have highlighted a rare occurrence of vaccine-induced immune thrombotic thrombocytopenia (VITT), also known as thrombotic thrombocytopenia syndrome (TTS), within 4–30 days following vaccination with certain COVID-19 vaccines. Scholars have proposed that the mechanism of VITT may be analogous to heparin-induced thrombocytopenia (HIT), involving the interaction of platelet factor 4 (PF4) antibodies [76]. In the case of VITT, the vaccine may act similarly to heparin in HIT, directly activating platelets. It has also been suggested that adenovirus vectors, spike proteins, mode of administration, and impurities could all potentially contribute to the development of VITT [77]. It is recommended to use non-heparin anticoagulants to reduce the formation of thrombi [78].

It is crucial to acknowledge that the risk of adverse effects on the cardiovascular system associated with infection with the SARS-CoV-2 is considerably higher than the risk of such effects following vaccination. Consequently, the rare risk of thrombosis and pericarditis should not dissuade individuals from receiving the vaccine [79].

5.5.1.7. Metformin. Previous study found that the use of metformin during the recovery period of COVID-19 infection significantly reduced post-COVID-19 condition by 41 %. Furthermore, the risk of post-COVID-19 condition was reduced by 63 % when metformin was administered within 4 days of the onset of symptoms of COVID-19 infection [80]. Mechanistically, metformin can reduce inflammation by attenuating the levels of NLRP3 inflammasome, IL-6, Th17 cells, macrophages, etc. [81] It may also interfere with the binding of SARS-COV-2 to the receptor, preserve microvascular responsiveness, and inhibit capillary permeability and plasminogen activator inhibitor-1 (PAI-1) [81]. However, it is recommended that patients with or without diabetes be treated with blood glucose monitoring and dose adjustments.

5.5.1.8. Immunotherapy. Researches have shown a negative correlation between inflammation, cytokine storm, and the prognosis of patients with long-term COVID-19 [17,82]. Therefore, for high-risk patients, it is recommended to take reasonable measures to reduce inflammation and cytokine levels. At present, the 10th edition of the COVID-19 Infection Diagnosis and Treatment Program recommends short-term use of glucocorticoids, interleukin-6 inhibitors and others to regulate the body's immunity.

5.5.1.9. Anti-SARS-COV-2 drugs. In the current therapeutic landscape, anti-SARS-CoV-2 drugs are categorized into several main

classes: RNA-dependent RNA-polymerase (RdRp) inhibitors, 3-chymotrypsin-like protease($3CL^{pro}$) and papain-like protease(PL^{pro}) inhibitors [83], Structural protein inhibitors [84]. Notably, 3CLpro and RdRp have emerged as the most extensively studied targets for SARS-CoV-2, exhibiting a high degree of conservation across coronaviruses, which has facilitated the development of broad-spectrum antiviral agents [83]. While drugs such as azvudine, molnupiravir, remdesivir, and Paxlovid, which are currently in widespread use, have been demonstrated to exhibit robust anti-SARS-CoV-2 activity within a relatively short timeframe [85–88], it is imperative to consider the potential impact of anti-SARS-CoV-2 drugs on perioperative cardiovascular risk.

Researches prior to the COVID-19 pandemic suggest that remdesivir can be metabolized to nucleotide adenosine, which triggers the release of catecholamines, including epinephrine. This mechanism has been linked to an increased risk of ventricular tachycardia, ventricular fibrillation, and atrial fibrillation. Paxlovid has also been implicated in potential bradycardia and sinus dysfunction, although the underlying mechanism remains elusive. Additionally, the concurrent administration of Paxlovid with antiplatelet agents such as ticagrelor, anticoagulants like warfarin, or direct oral anticoagulants such as rivaroxaban may heighten the risk of bleeding complications. Molnupiravir has been shown to elevate oxidative stress, potentially leading to tissue damage. Moreover, other pharmacological agents, including hydroxychloroquine and ivermectin, have been correlated with an increased risk of cardiovascular adverse events [89].

Furthermore, ritonavir, recognized as a potent inhibitor of cytochrome P450 (CYP450) [90], can impair the metabolism of various anesthetics and analgesics, including midazolam, fentanyl, and cardiotonic drugs such as amiodarone and quinidine. In contrast, etomidate, atracurium, remifentanil, and isoflurane are unaffected and can be preferentially used as anesthetic agents [91,92].For patients undergoing surgical procedures, alternative anti-SARS-CoV-2 agents such as azvudine or molnupiravir may be considered to mitigate the potential cardiovascular risk [42]. However, more evidence is needed to clarify the relationship between antivirals and perioperative cardiovascular risk.

5.5.2. Non-drug therapy

5.5.2.1. Nutritional support. Nutritional support is a crucial component of the comprehensive treatment for patients with long-term COVID-19. The Nutrition Risk Screening 2022 (NRS2022) and screening tool for the assessment of malnatrition in pediatrics (STAMP) can be used to assess the nutritional status of adult and pediatric patients, respectively. Based on the results of these scales, as well as the patient's gastrointestinal function and disease severity, a diet plan and appropriate nutritional supplements should be provided to ensure sufficient intake of energy, protein, and trace elements, which can promote recovery [93]. Studies have shown that animal foods, particularly red meat, can increase the body's inflammatory response. To reduce this risk, consider replacing some of the pork, beef, and lamb in your daily diet with deep-sea fish and soy products. Additionally, vitamin D deficiency is common in patients with cardiovascular disease (CVD). Supplementation with vitamin D can significantly reduce cardiovascular risk, especially in patients with low sun exposure [94]. Similarly, other nutrients such as vitamins A, B, and C, as well as zinc, iron, coenzyme Q10, and β-nicotinamide mononucleotide (NMN), can produce anti-oxidant effects, enhance immunity, and anti-viral effects [94,95], improving the nutritional status of the patients.

5.5.2.2. Exercise rehabilitation. When resuming exercise, it is important to strictly follow a gradual increase in intensity. Begin with breathing exercises, gentle stretching, and mild muscle strength training before moving on to aerobic training. It is recommended to perform aerobic exercise under supervision [96]. Studies have shown that supervised, tailored low-intensity and moderate-intensity synchronized training for resistance and endurance is a more effective, safer, and well-tolerated intervention that significantly improves fatigue, depression, heart function, cardiovascular health, and muscle strength [96,97].

5.5.2.3. Traditional Chinese medicine. The prevention of COVID-19 in traditional Chinese medicine focuses on enhancing the healthy 'qi', a Chinese medical theory, in the human body through methods such as cupping, acupuncture, and acupoint massage [98], to enhance patients' immunity and promote recovery.

5.5.2.4. Psychotherapy. long-term COVID-19 is a chronic disease that can cause symptoms such as fatigue and insomnia, significantly impacting patients' quality of life, which affects one-tenth of patients [99]. Therefore, psychotherapy is crucial in the recovery process for long-term COVID-19 patients. Psychotherapy can assist patients in managing stress, improving their psychological state, and enhancing their quality of life. Methods such as psychological counseling and cognitive-behavioral therapy can be applied. Additionally, psychotherapy emphasizes the significance of family and social support in helping patients develop confidence and approach their illness with a positive mindset [100].

6. Summary

Post-COVID-19 condition significantly increase perioperative cardiovascular risk. This risk should be assessed in a multidimensional way with respect to medical history, symptoms and physical examination, use of relevant ancillary tests, assessment of scales, and rehabilitation for better identification and prevention.We expect further researches to explore the link between COVID-19 infections and perioperative risk from Surgical and anesthetic perspectives.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Sixu Lai: Writing – original draft. **Su Min:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Covid coronavirus statistics worldometer. https://www.worldometers.Info.coronavirus, 2024. (Accessed 24 April 2024).
[2] L. The, Long covid: 3 years in, Lancet 401 (2023) 795.
[3] J.B. Soriano, S. Murthy, J.C. Marshall, P. Relan, J.V. Diaz, A clinical case definition of post-covid-19 condition by a delphi consensus, Lancet Infect. Dis. 22 (2022) e102–e107.
[4] S.M. Sidik, Heart disease after covid: what the data say, Nature 608 (2022) 26–28.
[5] Y. Xie, E. Xu, B. Bowe, Z. Al-Aly, Long-term cardiovascular outcomes of covid-19, Nat. Med. 28 (2022) 583–590.
[6] T.E.F. Abbott, A.J. Fowler, T.D. Dobbs, J. Gibson, T. Shahid, P. Dias, A. Akbari, I.S. Whitaker, R.M. Pearse, Mortality after surgery with SARS-cov-2 infection in england: a population-wide epidemiological study, Br. J. Anaesth. 127 (2021) 205–214.
[7] K. El Boghdadly, T.M. Cook, T. Goodacre, J. Kua, L. Blake, S. Denmark, S. Mcnally, N. Mercer, S.R. Moonesinghe, D.J. Summerton, SARS-cov-2 infection, covid-19 and timing of elective surgery, Anaesthesia 76 (2021) 940–946.
[8] E.Y.F. Wan, S. Mathur, R. Zhang, V.K.C. Yan, F.T.T. Lai, C.S.L. Chui, X. Li, C.K.H. Wong, E.W.Y. Chan, K.H. Yiu, et al., Association of covid-19 with short- and long-term risk of cardiovascular disease and mortality: a prospective cohort in UK biobank, Cardiovasc. Res. 119 (2023) 1718–1727.
[9] F. Doglietto, M. Vezzoli, F. Gheza, G.L. Lussardi, M. Domenicucci, L. Vecchiarelli, L. Zanin, G. Saraceno, L. Signorini, P.P. Panciani, et al., Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (covid-19) in Italy, JAMA Surg 155 (2020) 691.
[10] M.K. Chung, D.A. Zidar, M.R. Bristow, S.J. Cameron, T. Chan, C.V. Harding, D.H. Kwon, T. Singh, J.C. Tilton, E.J. Tsai, et al., Covid-19 and cardiovascular disease, Circ. Res. 128 (2021) 1214–1236.
[11] I. Hamming, W. Timens, M. Bulthuis, A.T. Lely, G.J. Navis, H. van Goor, Tissue distribution of ace2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis, J. Pathol. 203 (2004) 631–637.
[12] J.K. Salabei, Z.T. Asnake, Z.H. Ismail, K. Charles, G. Stanger, A.H. Abdullahi, A.T. Abraham, P. Okonoboh, Covid-19 and the cardiovascular system: an update, Am. J. Med. Sci. 364 (2022) 139–147.
[13] P. V Kovski, A. Kratzel, S. Steiner, H. Stalder, V. Thiel, Coronavirus biology and replication: implications for SARS-cov-2, Nat. Rev. Microbiol. 19 (2020) 155–170.
[14] J. Baggen, M. Jacquemyn, L. Persoons, E. Vanstreels, V.E. Pye, A.G. Wrobel, V. Calvaresi, S.R. Martin, C. Roustan, N.B. Cronin, et al., Tmem106b is a receptor mediating ace2-independent SARS-cov-2 cell entry, Cell 186 (2023) 3427–3442.
[15] Y. Gu, J. Cao, X. Zhang, H. Gao, Y. Wang, J. Wang, J. Zhang, G. Shen, X. Jiang, J. Yang, et al., Interaction Network of SARS-Cov-2 with Host Receptome through Spike Protein, Cold Spring Harbor Laboratory Press, 2020.
[16] S.S. Elsoukkary, M. Mostyka, A. Dillard, D.R. Berman, L.X. Ma, A. Chadburn, R.K. Yantiss, J. Jessurun, S.V. Seshan, A.C. Borczuk, A.C. Borczuk, et al., Autopsy findings in 32 patients with covid-19: a single-institution experience, Pathobiology 88 (2020) 56–68.
[17] Zhao, Hailian, et al., "SARS-CoV-2 RNA stabilizes host mRNAs to elicit immunopathogenesis.", Molecular cell. 84 (3) (2024) 490–505.e9, https://doi.org/10.1016/j.molcel.2023.11.032.
[18] N. Eberhardt, M.G. Noval, R. Kaur, L. Amadori, M. Gildea, S. Sajja, D. Das, B. Cilhoroz, O.J. Stewart, D.M. Fernandez, et al., SARS-cov-2 infection triggers pro-atherogenic inflammatory responses in human coronary vessels, Nature Cardiovascular Research 2 (2023) 899–916.
[19] J. Cheong, A. Ravishankar, S. Sharma, C.N. Parkhurst, S.A. Grassmann, C.K. Wingert, P. Laurent, S. Ma, L. Paddock, I.C. Miranda, et al., Epigenetic memory of coronavirus infection in innate immune cells and their progenitors, Cell 186 (2023) 3882–3902.
[20] B. Raman, C. Mccracken, M.P. Cassar, A.J. Moss, L. Finnigan, A.H.A. Samat, G. Ogbole, E.M. Tunnicliffe, F. Alfaro-Almagro, R. Menke, et al., Multiorgan mri findings after hospitalisation with covid-19 in the UK (c-more): a prospective, multicentre, observational cohort study, Lancet Respir. Med. 11 (2023) 1003–1019.
[21] Z. Shah, M. Rawat, C. Ng, E. Khan, R. Shah, S. Ashfaq, G. Bahader, Use of mesenchymal stem cell therapy in covid-19 related strokes, Neural Regen. Res. 0 (2023).
[22] S. Lei, F. Jiang, W. Su, C. Chen, J. Chen, W. Mei, L. Zhan, Y. Jia, L. Zhang, D. Liu, et al., Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of covid-19 infection, EClinicalMedicine 21 (2020) 100331.
[23] I. Katsoularis, H. Jerndal, S. Kalucza, K. Lindmark, O. Fonseca-Rodríguez, A.F. Connolly, Risk of arrhythmias following covid-19: nationwide self-controlled case series and matched cohort study, European Heart Journal Open 3 (2023).
[24] V.O. Puntmann, S. Martin, A. Shchendrygina, J. Hoffmann, M.M. Ka, E. Giokoglu, B. Vanchin, N. Holm, A. Karyou, G.S. Laux, et al., Long-term cardiac pathology in individuals with mild initial covid-19 illness, Nat. Med. 28 (2022) 2117–2123.
[25] L. Leng, J. Ma, P. Zhang, S. Xu, X. Li, Y. Jin, J. Cai, R. Tang, L. Zhao, Z. He, et al., Spatial region-resolved proteome map reveals mechanism of covid-19-associated heart injury, Cell Rep. 39 (2022) 110955.
[26] P. Severino, A. D'Amato, M. Pucci, F. Infusino, F. Adamo, L.I. Birtolo, L. Netti, G. Montefusco, C. Chimenti, C. Lavalle, et al., Ischemic heart disease pathophysiology paradigms overview: from plaque activation to microvascular dysfunction, Int. J. Mol. Sci. 21 (2020) 8118.
[27] A. Gąsecka, K.J. Filipiak, M.J. Jaguszewski, Impaired microcirculation function in covid-19 and implications for potential therapies, Cardiol. J. 27 (2020) 485–488.
[28] S.I. Bloom, M.T. Islam, L.A. Lesniewski, A.J. Donato, Mechanisms and consequences of endothelial cell senescence, Nat. Rev. Cardiol. 20 (2023) 38–51.
[29] M.A.M. Ali, S.A. Spinler, Covid-19 and thrombosis: from bench to bedside, Trends Cardiovasc. Med. 31 (2021) 143–160.
[30] D.A. Kasal, A. De Lorenzo, E. Tibiriçá, Covid-19 and microvascular disease: pathophysiology of SARS-cov-2 infection with focus on the renin-angiotensin system, Heart Lung Circ. 29 (2020) 1596–1602.
[31] H. Fogarty, L. Townsend, H. Morrin, A. Ahmad, C. Comerford, E. Karampini, H. Englert, M. Byrne, C. Bergin, J.M. O Sullivan, et al., Persistent endotheliopathy in the pathogenesis of long covid syndrome, J. Thromb. Haemostasis 19 (2021) 2546–2553.
[32] N.R. Smilowitz, J.S. Berger, Perioperative cardiovascular risk assessment and management for noncardiac surgery, JAMA 324 (2020) 279.

[33] G.A.L. Lurati Buse, C. Puelacher, D.M. Gualandro, A.S. Genini, R. Hidvegi, D. Bolliger, K. Arslani, L.A. Steiner, C. Kindler, C. Mueller, et al., Association between self-reported functional capacity and major adverse cardiac events in patients at elevated risk undergoing noncardiac surgery: a prospective diagnostic cohort study, Br. J. Anim. Behav. 126 (2021) 102–110.
[34] B. Raman, D.A. Bluemke, T.F. Lüscher, S. Neubauer, Long covid: post-acute sequelae of covid-19 with a cardiovascular focus, Eur. Heart J. 43 (2022) 1157–1172.
[35] D.F. Reilly, M.J. Mcneely, D. Doerner, D.L. Greenberg, T.O. Staiger, M.J. Geist, P.A. Vedovatti, J.E. Coffey, M.W. Mora, T.R. Johnson, et al., Self-reported exercise tolerance and the risk of serious perioperative complications, Arch. Intern. Med. 159 (1999) 2185–2192.
[36] N. Rohatgi, N.R. Smilowitz, R. Reejhsinghani, Perioperative cardiovascular considerations prior to elective noncardiac surgery in patients with a history of covid-19, JAMA Surg 157 (2022) 187.
[37] J. Cai, K. Lin, H. Zhang, Q. Xue, K. Zhu, G. Yuan, Y. Sun, F. Zhu, J. Ai, S. Wang, et al., A one-year follow-up study of systematic impact of long covid symptoms among patients post SARS-cov-2 omicron variants infection in shanghai, Emerg. Microb. Infect. 12 (2023) china.
[38] L.L. O'Mahoney, A. Routen, C. Gillies, W. Ekezie, A. Welford, A. Zhang, U. Karamchandani, N. Simms-Williams, S. Cassambai, A. Ardavani, et al., The prevalence and long-term health effects of long covid among hospitalised and non-hospitalised populations: a systematic review and meta-analysis, EClinicalMedicine 55 (2023) 101762.
[39] B. Bowe, Y. Xie, Z. Al-Aly, Postacute sequelae of covid-19 at 2 years, Nat. Med. 29 (2023) 2347–2357.
[40] T. Thaweethai, S.E. Jolley, E.W. Karlson, E.B. Levitan, B. Levy, G.A. Mccomsey, L. Mccorkell, G.N. Nadkarni, S. Parthasarathy, U. Singh, et al., Development of a definition of postacute sequelae of SARS-cov-2 infection, JAMA 329 (2023) 1934.
[41] T.J. Gluckman, N.M. Bhave, L.A. Allen, E.H. Chung, E.S. Spatz, E. Ammirati, A.L. Baggish, B. Bozkurt, W.K. Cornwell, K.G. Harmon, et al., 2022 acc expert consensus decision pathway on cardiovascular sequelae of covid-19 in adults: myocarditis and other myocardial involvement, post-acute sequelae of SARS-cov-2 infection, and return to play, J. Am. Coll. Cardiol. 79 (2022) 1717–1756.
[42] S. Halvorsen, J. Mehilli, S. Cassese, T.S. Hall, M. Abdelhamid, E. Barbato, S. De Hert, I. de Laval, T. Geisler, L. Hinterbuchner, et al., 2022 esc guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery, Eur. Heart J. 43 (2022) 3826–3924.
[43] P. Ladlow, D.A. Holdsworth, O. O Sullivan, R.M. Barker-Davies, A. Houston, R. Chamley, K. Rogers-Smith, V. Kinkaid, A. Kedzierski, J. Naylor, et al., (2023). Exercise tolerance, fatigue, mental health, and employment status at 5 and 12 months following covid-19 illness in a physically trained population, J. Appl. Physiol. 134 (1985) 622–637.
[44] W. Krahwinkel, T. Ketteler, J. Godke, J. Wolfertz, L.J. Ulbricht, I. Krakau, H. Gulker, Dobutamine stress echocardiography, Eur. Heart J. 18 (1997) 9–15.
[45] S.D. Kristensen, J. Knuuti, A. Saraste, S. Anker, H.E. B Tker, S.D. Hert, I. Ford, J.R. Gonzalez-Juanatey, B. Gorenek, G.R. Heyndrickx, et al., 2014 esc/esa guidelines on non-cardiac surgery: cardiovascular assessment and management: the joint task force on non-cardiac surgery: cardiovascular assessment and management of the european society of cardiology (esc) and the european society of anaesthesiology (esa), Eur. Heart J. 35 (2014) 2383–2431.
[46] B. Long, W.J. Brady, R.E. Bridwell, M. Ramzy, T. Montrief, M. Singh, M. Gottlieb, Electrocardiographic manifestations of covid-19, Am. J. Emerg. Med. 41 (2021) 96–103.
[47] M.M. Pinto-Filho, G.M. Paixão, P.R. Gomes, C.P.M. Soares, K. Singh, V.A. Rossi, F. Thienemann, C. Viljoen, B. Mohan, N. Sarrafzadegan, et al., Electrocardiographic findings and prognostic values in patients hospitalised with covid-19 in the world heart federation global study, Heart 109 (2022) 668–673.
[48] J. Kapusta, M. Babicki, K. Pieniawska śmiech, Ż. Kałuzińska Kołat, D. Kołat, P. Jankowski, J.D. Kasprzak, P. Wejner Mik, A. Bianek Bodzak, M. Chudzik, Clinical and electrocardiographic correlates of myocardial dysfunction after covid-19 in nonhospitalised patients in long-term follow-up. Data from the polish long-covid cardiovascular study, J. Med. Virol. 95 (2023).
[49] Y. Szekely, Y. Lichter, P. Taieb, A. Banai, A. Hochstadt, I. Merdler, A. Gal Oz, E. Rothschild, G. Baruch, Y. Peri, et al., Spectrum of cardiac manifestations in covid-19, Circulation 142 (2020) 342–353.
[50] B. Raman, D.A. Bluemke, T.F. L Scher, S. Neubauer, Long covid: post-acute sequelae of covid-19 with a cardiovascular focus, Eur. Heart J. 43 (2022) 1157–1172.
[51] A.N. Koshy, F.J. Ha, P.J. Gow, H.C. Han, F.M. Amirul-Islam, H.S. Lim, A.W. Teh, O. Farouque, Computed tomographic coronary angiography in risk stratification prior to non-cardiac surgery: a systematic review and meta-analysis, Heart 105 (2019) 1335–1342.
[52] J. Ahn, J.R. Park, J.H. Min, J. Sohn, S. Hwang, Y. Park, J. Koh, Y. Jeong, C.H. Kwak, J. Hwang, Risk stratification using computed tomography coronary angiography in patients undergoing intermediate-risk noncardiac surgery, J. Am. Coll. Cardiol. 61 (2013) 661–668.
[53] T. Sheth, M. Chan, C. Butler, B. Chow, V. Tandon, P. Nagele, A. Mitha, M. Mrkobrada, W. Szczeklik, Y. Faridah, et al., Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery: prospective cohort study, BMJ 350 (2015) h1907.
[54] V.M. Ferreira, J. Schulz-Menger, G. Holmvang, C.M. Kramer, I. Carbone, U. Sechtem, I. Kindermann, M. Gutberlet, L.T. Cooper, P. Liu, et al., Cardiovascular magnetic resonance in nonischemic myocardial inflammation, J. Am. Coll. Cardiol. 72 (2018) 3158–3176.
[55] D.E. Clark, J.M. Dendy, D.L. Li, K. Crum, D. Dixon, K. George-Durrett, A.P. Parikh, J.W. Wassenaar, S.G. Hughes, J.H. Soslow, Cardiovascular magnetic resonance evaluation of soldiers after recovery from symptomatic SARS-cov-2 infection: a case–control study of cardiovascular post-acute sequelae of SARS-cov-2 infection (cv pasc), J. Cardiovasc. Magn. Reson. 23 (2021).
[56] S.J. Yong, A. Halim, M. Halim, S. Liu, M. Aljeldah, B.R. Al Shammari, S. Alwarthan, M. Alhajri, A. Alawfi, A. Alshengeti, et al., Inflammatory and vascular biomarkers in post-covid-19 syndrome: a systematic review and meta-analysis of over 20 biomarkers, Rev. Med. Virol. 33 (2023).
[57] L. De Michieli, A.S. Jaffe, Y. Sandoval, Use and prognostic implications of cardiac troponin in covid-19. Cardiol, Clin. 40 (2022) 287–300.
[58] D. Cozzolino, C. Romano, C. Sardu, R. Nevola, G.R. Umano, L. Rinaldi, L.E. Adinolfi, C. Catalini, A. Marrone, M. Municinò, et al., Long-term prognosis among covid-19 patients: the predictive role played by hyperinflammation and arrhythmic disorders in fatal outcome, J. Clin. Med. 12 (2023) 5691.
[59] D. Phelan, J.H. Kim, M.D. Elliott, M.M. Wasfy, P. Cremer, A.M. Johri, M.S. Emery, P.P. Sengupta, S. Sharma, M.W. Martinez, et al., Screening of potential cardiac involvement in competitive athletes recovering from covid-19, JACC (J. Am. Coll. Cardiol.): Cardiovascular Imaging 13 (2020) 2635–2652.
[60] N.M. Dixit, A. Churchill, A. Nsair, J.J. Hsu, Post-acute covid-19 syndrome and the cardiovascular system: what is known? Am. Heart J.: Cardiol. Res. Pract. 5 (2021) 100025.
[61] R.D. Mitrani, N. Dabas, J.J. Goldberger, Covid-19 cardiac injury: implications for long-term surveillance and outcomes in survivors, Heart Rhythm 17 (2020) 1984–1990.
[62] M. Gyöngyösi, P. Alcaide, F.W. Asselbergs, B.J.J.M. Brundel, G.G. Camici, P.D.C. Martins, P. Ferdinandy, M. Fontana, H. Girao, M. Gnecchi, et al., Long covid and the cardiovascular system—elucidating causes and cellular mechanisms in order to develop targeted diagnostic and therapeutic strategies: a joint scientific statement of the esc working groups on cellular biology of the heart and myocardial and pericardial diseases, Cardiovasc. Res. 119 (2022) 336–356.
[63] W.J. Flu, J.P. van Kuijk, M. Chonchol, T.A. Winkel, H.J. Verhagen, J.J. Bax, D. Poldermans, Timing of pre-operative beta-blocker treatment in vascular surgery patients: influence on post-operative outcome, J. Am. Coll. Cardiol. 56 (2010) 1922–1929.
[64] H. Blessberger, S.R. Lewis, M.W. Pritchard, L.J. Fawcett, H. Domanovits, O. Schlager, B. Wildner, J. Kammler, C. Steinwender, Perioperative beta-blockers for preventing surgery-related mortality and morbidity in adults undergoing cardiac surgery, Cochrane Database Syst. Rev. 9 (2019) CD13435.
[65] O. Berwanger, E.S.P. de Barros, R.R. Barbosa, D.B. Precoma, E.L. Figueiredo, L.A. Hajjar, C.D. Kruel, C. Alboim, A.P. Almeida, M.D. Dracoulakis, et al., Atorvastatin for high-risk statin-naïve patients undergoing noncardiac surgery: the lowering the risk of operative complications using atorvastatin loading dose (load) randomized trial, Am. Heart J. 184 (2017) 88–96.
[66] S.D. Kristensen, J. Knuuti, A. Saraste, S. Anker, H.E. Bøtker, S.D. Hert, I. Ford, J.R. Gonzalez-Juanatey, B. Gorenek, G.R. Heyndrickx, et al., 2014 esc/esa guidelines on non-cardiac surgery: cardiovascular assessment and management: the joint task force on non-cardiac surgery: cardiovascular assessment and management of the european society of cardiology (esc) and the european society of anaesthesiology (esa), Eur. Heart J. 35 (2014) 2383–2431.
[67] N. Perico, M. Cortinovis, F. Suter, G. Remuzzi, Home as the new frontier for the treatment of covid-19: the case for anti-inflammatory agents, Lancet Infect. Dis. 23 (2023) e22–e33.

[68] E. Pretorius, M. Vlok, C. Venter, J.A. Bezuidenhout, G.J. Laubscher, J. Steenkamp, D.B. Kell, Persistent clotting protein pathology in long covid/post-acute sequelae of covid-19 (pasc) is accompanied by increased levels of antiplasmin, Cardiovasc. Diabetol. 20 (2021).
[69] H.C. Kwaan, P.F. Lindholm, The central role of fibrinolytic response in covid-19—a hematologist's perspective, Int. J. Mol. Sci. 22 (2021) 1283.
[70] R.D. Lopes, A.V.S. Macedo, P.G.M. de Barros E Silva, R.J. Moll-Bernardes, A. Feldman, G. D'Andréa Saba Arruda, A.S. de Souza, D.C. de Albuquerque, L. Mazza, M.F. Santos, et al., Continuing versus suspending angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: impact on adverse outcomes in hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-cov-2)–the brace corona trial, Am. Heart J. 226 (2020) 49–59.
[71] E. Cojocaru, C. Cojocaru, C. Vlad, L. Eva, Role of the renin-angiotensin system in long covid's cardiovascular injuries, Biomedicines 11 (2023) 2004.
[72] W.D. Strain, O. Sherwood, A. Banerjee, V. Van der Togt, L. Hishmeh, J. Rossman, The impact of covid vaccination on symptoms of long covid: an international survey of people with lived experience of long covid, Vaccines 10 (2022) 652.
[73] M. Levine-Tiefenbrun, I. Yelin, R. Katz, E. Herzel, Z. Golan, L. Schreiber, T. Wolf, V. Nadler, A. Ben-Tov, J. Kuint, et al., Initial report of decreased SARS-cov-2 viral load after inoculation with the bnt162b2 vaccine, Nat. Med. 27 (2021) 790–792.
[74] E. Lazarou, P. Tsioufis, C. Vlachopoulos, C. Tsioufis, G. Lazaros, Acute pericarditis: update, Curr. Cardiol. Rep. 24 (2022) 905–913.
[75] A. Buoninfante, A. Andeweg, G. Genov, M. Cavaleri, Myocarditis associated with covid-19 vaccination, NPJ Vaccines 9 (2024) 122.
[76] A.J. Kanack, A. Padmanabhan, Vaccine-induced immune thrombotic thrombocytopenia. Best practice & research, Clinical haematology 35 (2022) 101381.
[77] H. Ledford, Covid vaccines and blood clots: what researchers know so far, Nature 596 (2021) 479–481.
[78] S.M.H. Atyabi, F. Rommasi, M.H. Ramezani, M.F. Ghane Ezabadi, M.A. Arani, M.H. Sadeghi, M.M. Ahmed, A. Rajabi, N. Dehghan, A. Sohrabi, et al., Relationship between blood clots and covid-19 vaccines: a literature review, Open Life Sci. 17 (2022) 401–415.
[79] C.L. Lau, I. Galea, Risk-benefit analysis of covid-19 vaccines - a neurological perspective, Nat. Rev. Neurol. 18 (2022) 69–70.
[80] C.T. Bramante, J.B. Buse, D.M. Liebovitz, J.M. Nicklas, M.A. Puskarich, K. Cohen, H.K. Belani, B.J. Anderson, J.D. Huling, C.J. Tignanelli, et al., Outpatient treatment of covid-19 and incidence of post-covid-19 condition over 10 months (covid-out): a multicentre, randomised, quadruple-blind, parallel-group, phase 3 trial, Lancet Infect. Dis. 23 (2023) 1119–1129.
[81] N. Wiernsperger, A. Al-Salameh, B. Cariou, J. Lalau, Protection by metformin against severe covid-19: an in-depth mechanistic analysis, Diabetes & Metabolism 48 (2022) 101359.
[82] E. Gusev, A. Sarapultsev, L. Solomatina, V. Chereshnev, SARS-cov-2-specific immune response and the pathogenesis of covid-19, Int. J. Mol. Sci. 23 (2022) 1716.
[83] R. Cannalire, C. Cerchia, A.R. Beccari, F.S. Di Leva, V. Summa, Targeting SARS-cov-2 proteases and polymerase for covid-19 treatment: state of the art and future opportunities, J. Med. Chem. 65 (2022) 2716–2746.
[84] S. Jean, P. Lee, P. Hsueh, Treatment options for covid-19: the reality and challenges, Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi 53 (2020) 436–443.
[85] F. Ader, M. Bouscambert-Duchamp, M. Hites, N. Peiffer-Smadja, J. Poissy, D. Belhadi, A. Diallo, M. Lê, G. Peytavin, T. Staub, et al., Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with covid-19 (discovery): a phase 3, randomised, controlled, open-label trial, Lancet Infect. Dis. 22 (2022) 209–221.
[86] J. Zhang, Y. Li, L. Wang, H. Liu, S. Lu, Y. Liu, K. Li, B. Liu, S. Li, F. Shao, et al., Azvudine is a thymus-homing anti-SARS-cov-2 drug effective in treating covid-19 patients, Signal Transduct. Target. Ther. 6 (2021) 414.
[87] S. Dryden-Peterson, A. Kim, A.Y. Kim, E.C. Caniglia, I.T. Lennes, R. Patel, L. Gainer, L. Dutton, E. Donahue, R.T. Gandhi, et al., Nirmatrelvir plus ritonavir for early covid-19 in a large u.s. Health system : a population-based cohort study, Ann. Intern. Med. 176 (2023) 77–84.
[88] A. Wahl, L.E. Gralinski, C.E. Johnson, W. Yao, M. Kovarova, K.H.R. Dinnon, H. Liu, V.J. Madden, H.M. Krzystek, C. De, et al., SARS-cov-2 infection is effectively treated and prevented by eidd-2801, Nature 591 (2021) 451–457.
[89] Eileen Chen, Xi Lei, Cardiovascular adverse effects of antiviral therapies for COVID-19: Evidence and plausible mechanisms, Acta Pharmacol. Sin. (2024), https://doi.org/10.1038/s41401-024-01382-w, 9 Sep.
[90] P. Pagliano, A. Spera, C. Sellitto, G. Scarpati, V. Folliero, O. Piazza, G. Franci, V. Conti, T. Ascione, Preclinical discovery and development of nirmatrelvir/ritonavir combinational therapy for the treatment of covid-19 and the lessons learned from SARS-cov-2 variants, Expert. Opin. Drug Discov. 18 (2023) 1301–1311.
[91] M. Deodhar, S.B. Al Rihani, M.J. Arwood, L. Darakjian, P. Dow, J. Turgeon, V. Michaud, Mechanisms of cyp450 inhibition: understanding drug-drug interactions due to mechanism-based inhibition in clinical practice, Pharmaceutics 12 (2020) 846.
[92] R. Böhm, K. Reinecke, B. Bein, [Anesthetic drug interactions], Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie : AINS 49 (2014), 316-324, 325.
[93] A. Tsagari, G. Risvas, J.V. Papathanasiou, Y. Dionyssiotis, Nutritional management of individuals with SARS-cov-2 infection during rehabilitation, Journal of Frailty, Sarcopenia and Falls 7 (2022) 88–94.
[94] L. Barrea, W.B. Grant, E. Frias-Toral, C. Vetrani, L. Verde, G. de Alteriis, A. Docimo, S. Savastano, A. Colao, G. Muscogiuri, Dietary recommendations for post-covid-19 syndrome, Nutrients 14 (2022) 1305.
[95] J. Yoshino, J.A. Baur, S. Imai, Nad+ intermediates: the biology and therapeutic potential of nmn and nr, Cell Metab 27 (2018) 513–528.
[96] A. Jimeno Almazán, F. Franco López, Á. Buendía Romero, A. Martínez Cava, J.A. Sánchez Agar, B.J. Sánchez Alcaraz Martínez, J. Courel Ibáñez, J.G. Pallarés, Rehabilitation for<SCP>post-covid </SCP>-19 condition through a supervised exercise intervention: a randomized controlled trial, Scand. J. Med. Sci. Sports 32 (2022) 1791–1801.
[97] M. Halle, W. Bloch, A.M. Niess, H.G. Predel, C. Reinsberger, J. Scharhag, J. Steinacker, B. Wolfarth, J. Scherr, J. Niebauer, Exercise and sports after covid-19—guidance from a clinical perspective. Transl, Sports Med. 4 (2021) 310–318.
[98] N.H.C.O. Prc, N.A.O.T. Medicine, 新型冠状病毒感染诊疗方案(试行第十版), 传染病信息 36 (2023) 18–25.
[99] Y. Zhao, L. Shi, Z. Jiang, N. Zeng, H. Mei, Y. Lu, J. Yang, F. Jin, S. Ni, S. Wu, et al., The phenotype and prediction of long-term physical, mental and cognitive covid-19 sequelae 20 months after recovery, a community-based cohort study in China, Mol. Psychiatry 28 (2023) 1793–1801.
[100] H. Löffler-Stastka, M. Pietrzak-Franger, Covid-19 survivors: multi-disciplinary efforts in psychiatry and medical humanities for long-term realignment, World J. Psychiatry 12 (2022) 995–998.