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The negative effects of long COVID-19 on cardiovascular health and implications for the presurgical examination

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Abstract

Context: In 2019, emergence of the novel and communicable severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection took scientific communities by surprise and imposed significant burden on healthcare systems globally. Although the advent of this disease piqued the interest of academic centers, healthcare systems, and the general public, there is still much yet to be elucidated regarding epidemiology, pathophysiology, and long-term impacts of coronavirus disease 2019 (COVID-19). It has been established that long COVID-19 can impact multiple organ systems, including the cardiovascular system, unfavorably. Although the pathophysiology of this damage is not well understood, adverse sequelae may range from chest pain and arrhythmias to heart failure (HF), myocardial infarction, or sudden cardiac death. For any postacute COVID-19 patient requiring a surgical procedure, the potential for cardiac injury secondary to long COVID-19 must be considered in the preoperative cardiac examination.

Objectives: This literature review serves to add to the growing body of literature exploring postacute cardiovascular outcomes of COVID-19, with a focus on presurgical cardiac clearance in the adult patient. Specifically, this review studies the prevalence of cardiovascular symptomatology including chest pain, arrhythmias, blood pressure changes, myo-/pericarditis, HF, cardiomyopathy, orthostatic intolerance, and thromboembolism. Although current evidence is scarce in both quality and quantity, it is the goal that this review will highlight the negative impacts of long COVID-19 on cardiovascular health and encourage providers

to be cognizant of potential sequelae in the context of the presurgical examination.

Methods: For this study, peer-reviewed and journal-published articles were selected based on established inclusion and exclusion criteria to address the question “How does long COVID-19 impact the presurgical cardiac examination of an adult scheduled to undergo a noncardiac procedure?” Inclusion criteria included human studies conducted in adult patients and published in peer-reviewed journals up until May 2024 examining the effects of long-COVID-19 infection on the cardiovascular system. Exclusion criteria eliminated unpublished reports, preprints, duplicate articles, literature regarding coronavirus strains other than COVID-19, studies regarding post-COVID-19 vaccination complications, animal studies, and studies conducted in people younger than 18 years of age. A total of 6,675 studies were retrieved from PubMed and Google Scholar. Following screening, 60 studies were included in final consideration.

Results: Cardiovascular symptoms of postacute COVID-19 infection were encountered with the following percentages prevalence (total numbers of articles mentioning symptom/total number of articles [60]): chest pain (83.3), arrhythmias (88.3), hypertension (40.0), hypotension (16.7), myocarditis (80.0), pericarditis (51.7), HF (70.0), cardiomyopathy (55.0), orthostatic intolerance (56.7), and thromboembolic events (85.0).

Conclusions: The presence of persisting COVID symptoms may negatively impact the patient’s physical examination, blood tests, electrocardiogram (ECG), imaging, and/or echocardiogram. Cardiac conditions associated with long COVID require special attention in the context of the presurgical candidate due to an increased risk of sudden cardiac death, myocarditis, stroke, and myocardial infarction – even in those who were healthy prior to acute COVID-19 infection. Until more specific scientific evidence comes to light, care of these patients should be viewed through the prism of the best practices already in use and clinicians should maintain a low threshold to pursue more extensive cardiac workup prior to surgery.

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According to the American College of Surgeons, approximately 15 million Americans have some type of surgery every year. Among these procedures, major adverse cardiac events (MACEs) account for a large portion of perioperative events contributing to significant morbidity and increasing surgical mortality [1]. To reduce the potential for surgical risk and to prevent lasting cardiac complications, patients are subject to presurgical risk evaluation and stratification that considers both patient- and procedure-specific factors. This workup may include imaging, laboratory testing, electrocardiography (ECG), and/or more focused investigation. Selection of ordered tests and workup should depend on patient history, coexisting medical conditions, and physical examination.

Although there is not one standardized set of guidelines utilized to evaluate cardiovascular risk in any presurgical candidate, the preoperative cardiac risk assessment written by the American College of Cardiology/American Heart Association (ACC/AHA) is commonly employed in the United States. This algorithm integrates clinical predictors from patient history and physical examination to guide recommendations. The presence of certain predictors including unstable angina, recent myocardial infarction, decompensated heart failure (HF), arrhythmias, and valvular disease may prompt the surgeon to delay or postpone an elective procedure until further cardiac workup is pursued [2]. Even though perioperative cardiac events are a well-known danger of surgery, there is a multitude of cardiovascular factors contributing to this overall risk burden that are still not fully understood.

With the recent emergence of the 2019 novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) infection, the incidence of cardiac maladies has increased exponentially. In the time since the onset of coronavirus disease 2019 (COVID-19), it has been established that the impacts of COVID-19 do not solely affect the respiratory system but may also impair the cardiovascular system. We as a scientific community have established that cardiovascular injury including, but not limited to, chest pain, arrhythmias, HF, and cardiac inflammatory conditions, is common during the acute phase of COVID-19 and is associated with worse short-term outcomes. Furthermore, long-term follow-up has demonstrated higher rates of arrhythmia, ischemic heart disease, HF, and thrombotic disorders in those with a history of acute COVID-19 infection [3]. As COVID-19 continues to spread communicably throughout communities, incidence may prove to be a harbinger for increase in global cardiovascular disease burden. Future studies are needed to elucidate the extent of cardiac involvement in acute COVID-19 infection.

This study, however, focuses on the cardiovascular sequelae of the clinical state succeeding the acute phase of infection.

The phenomenon of new-onset symptoms following acute infection or persisting into recovery, known generally as “long COVID,” has become a worldwide, noncommunicable epidemic, caused by long-lasting multiorgan symptoms that may persist for weeks or even months after acute COVID-19 infection has subsided [4]. In addition to the complications observed to date, there is still much that we have not yet discovered about the lasting impacts following the acute phase of COVID-19 infection and how they might impact the presurgical candidate.

Given the millions of acute infections in the United States since the onset in 2019, perioperative providers are expected to encounter COVID “long-haulers” in increasing numbers. Cardiovascular symptoms of long COVID-19 do not need to be minimized because these patients present an increased risk for perioperative morbidity and mortality for up to 7 weeks after initial illness [5]. There are currently no standardized recommendations to guide surgeons and primary care physicians in performing a presurgical cardiac examination for these patients due to the recency of the disease and the still fragmentary understanding of long COVID-19. It is important to acknowledge that there is no perfect solution given the ongoing uncertainty of long COVID and the varying availability of resources globally including, but not limited to, cardiopulmonary investigation and perioperative research.

The purpose of this report is to highlight what is known about the long-term cardiovascular sequelae of COVID-19 and implications on the presurgical cardiac evaluation in an adult patient. This review will serve to summarize cardiovascular sequelae of long COVID-19 infection based on the published literature and theorize how these manifestations may affect the cardiac fitness of the presurgical candidate. The following symptoms will be addressed: chest pain, arrhythmias, hypertension, hypotension, thromboembolic events, myocarditis, pericarditis, HF, orthostatic intolerance, and cardiomyopathy. Put simply, this review will address the question, “How does long COVID-19 impact the presurgical cardiac examination of an adult scheduled to undergo a noncardiac procedure?”

Background

The coronavirus disease 2019 (COVID-19) pandemic is a global outbreak of a novel coronavirus caused by SARS-CoV-2 first identified in December 2019. This widespread and pervasive illness is responsible for significant morbidity and mortality, accounting for more than 7 million deaths globally since its onset [6]. Repercussions of this illness have presented substantial challenges for healthcare systems around the world.

Table 1: Various definitions of long COVID-19 [8–10].

Organization	Definition
World Health Organization (WHO) [8]	“The continuation or development of new symptoms 3 months after the initial SARS-CoV-2 infection, with these symptoms lasting for at least 2 months with no other explanation.”
Centers for Disease Control and Prevention (CDC) [9]	“Signs, symptoms, and conditions that continue to develop after initial SARS-CoV-2 infection. The signs, symptoms, and conditions are present 4 weeks or more after the initial phase of infection; may be multi-systemic; and may present with a relapsing–remitting pattern or progression or worsen over time, with the possibility of severe and life-threatening events even months or years after infection.”
National Institutes of Health (NIH) [10]	“The health problems that some people experience a few months after a COVID-19 diagnosis.”

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

As previously mentioned, it has since been shown that acute COVID-19 infection is a complex inflammatory disease that has the potential for multisystemic injury. Thus, this virus can adversely impact not just the respiratory system, but also the cardiopulmonary, hematologic, neurologic, gastrointestinal, and endocrine systems, among others.

In recent years, there has been increasing evidence of long-term complications following recovery from acute COVID-19 infection. Despite a full recovery, a large population of COVID-19 patients displays a broad spectrum of symptoms with multisystemic effects. Evidence suggests that clinical symptomatology in long COVID is overlapping with, yet clinically distinct from, acute COVID-19 infection and could persist in patients who have recovered for weeks to months, thus adding to the overall disease burden [7]. Thus, there is marked heterogeneity in both the short- and long-term manifestations of COVID-19. A universally accepted definition for long COVID-19 has yet to be established. Table 1 shows some of the varying definitions across major global health associations. Irrespective of which definition is appreciated, it is important to recognize that long COVID affects survivors of all disease severity. Long COVID may develop in patients with widely varying acute phase presentations, ranging from asymptomatic infection to critical illness. Unlike symptoms following the critical illness or acute phases of other coronavirus infections, symptoms of long COVID-19 are commonly reported in individuals with a low risk for COVID-19–related mortality such as patients who are young with no chronic comorbidities [11]. While global health strategies, vaccines, and various pharmacologic therapies have significantly reduced the incidence of COVID-19 mortality and critical illness, the long-term consequences of the disease are still not fully known. A more comprehensive understanding of this disease process is crucial for providing appropriate evidence-based patient care. Future studies on this topic will contribute to patient-specific care and help guide clinicians in assessing the cardiac fitness of the presurgical candidate.

Epidemiology

Because COVID-19 is so new, research to this point has been based on a relatively short observation period, and the epidemiology of long COVID is not yet well defined. According to Dennis et al. [11], among those surviving acute COVID-19 infection, 10 % report persistent symptoms for 12 weeks or longer after initial infection. As time goes on and more cases of long COVID present, it is safe to infer that the burden on healthcare systems will grow as well. This positive correlation highlights the need for ongoing research to quantify and qualify the multiple dimensions of this disease.

Risk factors

Although not the focus of this review, it would be prudent to mention risk factors that have been studied for their contribution in the development of long COVID-19. It has been established that long COVID can affect those with all severity of acute disease and irrespective of existing comorbidities [11]. However, the severity of the initial illness is associated most strongly with long-term sequelae, thus putting those with severe acute disease and those requiring intensive care at the highest risk. According to the *Journal of Cardiothoracic and Vascular Anesthesia*, other factors that were associated with long-term sequelae include: “higher BMI, respiratory disease, older age, female sex, Black/Asian/minority ethnicities, ... abnormal radiologic findings, reduced quality-of-life scores, and decreased pulmonary function on spirometry found on follow-up after acute disease” [5]. In the presence of these risk factors, the physician performing the presurgical cardiac examination should be all the more vigilant and maintain a low threshold to perform further cardiac workup in order to maximize perioperative patient safety.

Methods

Study protocol

This systematic review was conducted in accordance with the recommendations outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [12].

Information sources and search methodology

The research question prompting this study is: “How does long COVID-19 impact the presurgical cardiac examination of an adult scheduled to undergo a noncardiac procedure?” To guide the identification of appropriate key terms and employ effective search strategies to guide the search of bibliographic databases, the research question was framed into the population, exposure, outcome (PEO) model. These criteria included: (1) peer-reviewed and journal-published literature including cases and reviews discussing long-term cardiovascular COVID-19 effects in adults as the population under study; (2) studies that focused primarily on adults experiencing symptomatology of COVID-19 (SARS-CoV-2) infection now in the postacute or convalescent phases as the exposure; and (3) outcome measures including those studies that discussed cardiovascular complications of long COVID-19 infection.

Inclusion criteria

The inclusion criteria were: (1) English-language studies published in peer-reviewed journals up until May 2024 that examined the effects of long COVID-19 infection on the cardiovascular system; (2) human studies; and (3) studies conducted in adult populations.

Articles that did not consider long COVID in the context of the cardiovascular system, such as studies regarding acute COVID-19 infection and/or long COVID-19 prevention, diagnosis, or treatment, were not included. Literature that was neither peer-reviewed nor journal-published in English were excluded.

Exclusion criteria

The exclusion criteria were as follows: (1) studies not available in English; (2) unpublished reports, preprints, or duplicate articles; (3) literature regarding coronavirus

strains other than COVID-19; (4) studies regarding post-COVID-19 vaccination complications; (5) animal studies; and (6) studies conducted in people younger than 18 years of age.

Overall, the eligibility criteria established a detailed and effective search for pertinent studies and inclusion of reliable data to support findings. With this strategy, the review is more meticulous and reliable, and the conclusions are more accurate.

Study design and data collection

For the purpose of this study, we thoroughly searched two databases – PubMed and Google Scholar – during the months of April and May 2024.

Our initial search integrated the following key terms: “Long COVID, long COVID-19, long-haul COVID, postacute sequelae of SARS-CoV-2 infection” and “cardiac, cardiovascular, effects on heart” in the title or abstract. Between the two databases, there was a total of 6,675 relevant articles retrieved.

One reviewer (H.S.) independently screened articles for inclusion on the basis of the previously mentioned inclusion/exclusion criteria and taking into consideration the employed PEO structure.

Because this study is a review of previously published literature, the risk of bias associated with included literature was not assessed.

Ethical clearance and approval from the Institutional Review Board was not required because all data extrapolated for the purpose of this study was derived from already-published studies. No patients or members of the public were consented, interviewed directly, or involved in the present research. No funding was given or received for this study.

Study selection

During the initial data search, 6,675 records were collected. The retrieved studies from bibliographic databases were then entered into Rayyan electronic software [13], where duplicate articles were flagged and then removed manually. After the removal of duplicates, 5,279 articles were kept for consideration. Among the remaining articles, 2,070 studies were marked as ineligible by automation. After preliminary screening of the titles and abstracts of the selected studies, 98 articles were selected. Among these 98 articles, 7 articles were not able to be retrieved.

In order to determine if the remaining articles met the chosen inclusion/exclusion criteria for this review, 91

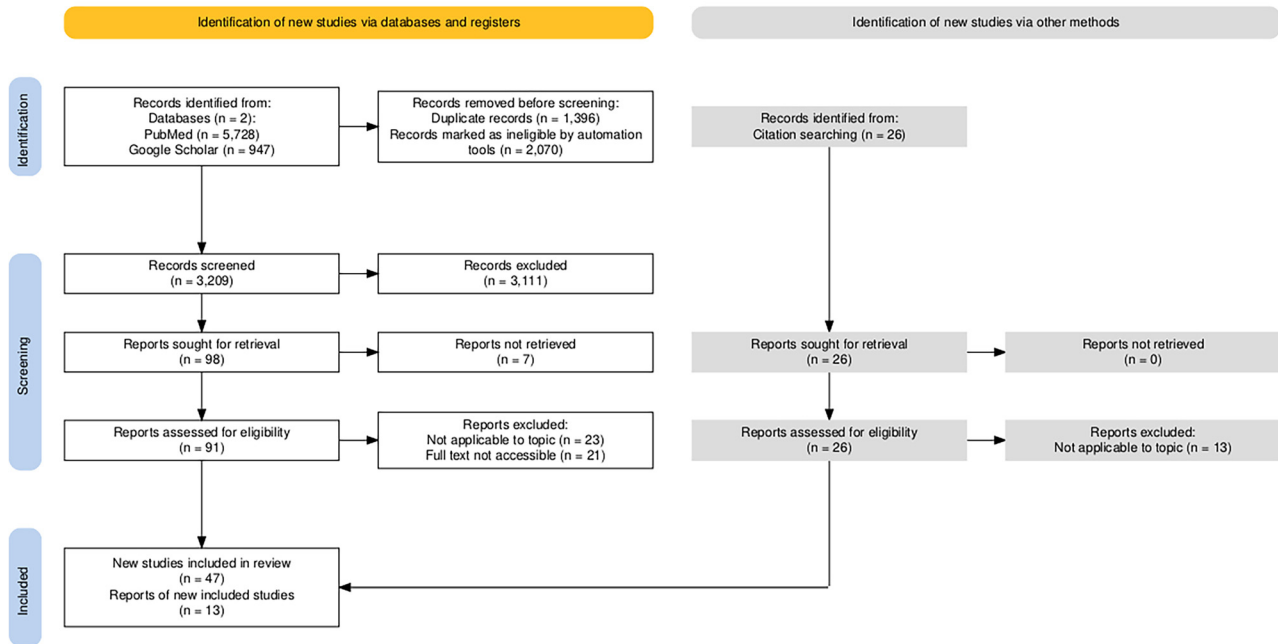


Figure 1: Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow chart [12].

potentially pertinent studies were designated for full-text review. After removing articles in which the full-text version of the article was not accessible and those that were not pertinent to the research question of this review, 47 articles were evaluated as eligible. From these studies, an additional 26 citations were appraised for inclusion. Among these, 13 new studies that are reports were included. After exclusion, there were 60 studies utilized to inform the direction of this review. Final study selection was made based on study quality and the satisfaction of the eligibility criteria. Figure 1 demonstrates the process of study selection in the form of a PRISMA flow chart [12].

Results

Selected articles were analyzed for the mention of symptomatology pertaining to the following categories: (1) chest pain, (2) arrhythmias, (3) blood pressure changes, (4) myocarditis/pericarditis, (5) HF, (6), cardiomyopathy, (7) orthostatic intolerance, and (8) thromboembolic events. The prevalence of symptoms mentioned in the studies is represented in Figure 2, which demonstrates the number of times that the specific symptom was encountered across the assessed articles. The percentage of the total number of symptoms mentioned for which each of these categories accounts is portrayed in Figure 3. This chart takes the combined total of symptoms mentioned and then determines

the percentage of the total that is made up by each given symptom. Appendix A demonstrates the raw data collected from the literature review. Supplementary Table 1 lists all of the symptoms and their corresponding references.

Chest pain

Of the 60 evaluated articles, chest pain was one of the most prominent long-term cardiovascular sequelae of COVID-19 infection, presenting in 50 (83.3 %) of total reviewed articles. Of the mentioned long-term sequelae of COVID-19 extrapolated from included literature, chest pain comprised 13.30 % of the symptom burden. It is important to note that the etiology of postacute COVID-19 chest pain may be either musculoskeletal or cardiovascular in nature. For the purpose of this analysis, all reported occurrences of chest pain were taken into statistical consideration.

Arrhythmias

Another prominent symptom discussed in the selected articles was cardiac arrhythmia. Of the 60 articles, 53 (88.3 %) described some type of cardiac arrhythmia. Arrhythmia accounts for 14.10 % of all mentioned symptoms. Of the ECG abnormalities described, new-onset atrial fibrillation was the most prevalent (21 articles). Additional atrial arrhythmias included atrial flutter (8 articles). Ventricular

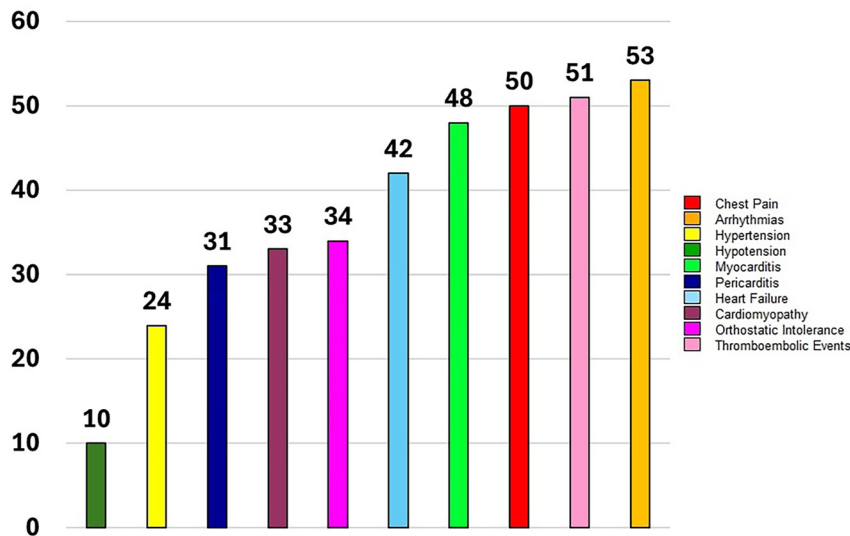


Figure 2: The prevalence of symptoms mentioned in the reviewed literature [4, 5, 7, 11, 14–70].

arrhythmias were not as frequently reported (13 articles). Of the discussed ventricular arrhythmias, nonsustained ventricular tachycardia had the highest incidence (9 articles). This was followed by premature ventricular contractions (7 articles) and ventricular fibrillation (4 articles). The prevalence of the specific type of arrhythmia in relation to the total number of arrhythmias mentioned is portrayed in Supplementary Figure 1. In addition to specific cardiac arrhythmias, several articles made mention of palpitations (42 articles).

Blood pressure changes

The prevalence of blood pressure changes, inclusive of hypertension and hypotension, makes up 9.04 % of the total discussed symptoms. Hypertension and hypotension were conferred in 24 and 10 articles, respectively.

These data points represent mention of new-onset hypertension and hypotension irrespective of concomitant orthostatic intolerance.

Myocarditis/pericarditis

Together, myocarditis and pericarditis account for 21.01 % of the total mentioned symptoms. Myocarditis, including corresponding myocardial fibrosis, was encountered more frequently (48 articles), thus making up 12.77 % of the total symptom burden independent of pericarditis. In contrast, pericarditis was considered in 33 articles, making up a distinctive 8.24 % of the total symptoms.

Heart failure

Of the 60 evaluated articles, it was not uncommon for HF to be reported as a long-term sequela of COVID-19 infection. Making up 11.17 % of the total symptoms, HF was encountered in 42 articles.

Cardiomyopathy

Cardiomyopathy, inclusive of ischemic, nonischemic, and Takotsubo (stress) cardiomyopathy, accounted for 8.78 % of the total symptoms and was mentioned in 33 of the 60 reviewed articles.

To further break down the classifications of cardiomyopathy, ischemic cardiomyopathy, nonischemic cardiomyopathy, and stress cardiomyopathy were mentioned in 19, 12, and 9 articles, respectively. How each of these subtypes contributes to the total prevalence of post-COVID-19 cardiomyopathy is displayed in Supplementary Figure 2.

Orthostatic intolerance

For the purpose of this review, orthostatic intolerance syndrome has been defined as encompassing orthostatic hypotension, postural orthostatic tachycardia syndrome (POTS), and vasovagal syncope. There were 34 articles that identified orthostatic intolerance as a cardiovascular manifestation of long COVID-19. This made up 9.04 % of the total extrapolated symptomatology.

In addition to orthostatic intolerance as an umbrella term, POTS was frequently mentioned independently (31 articles).

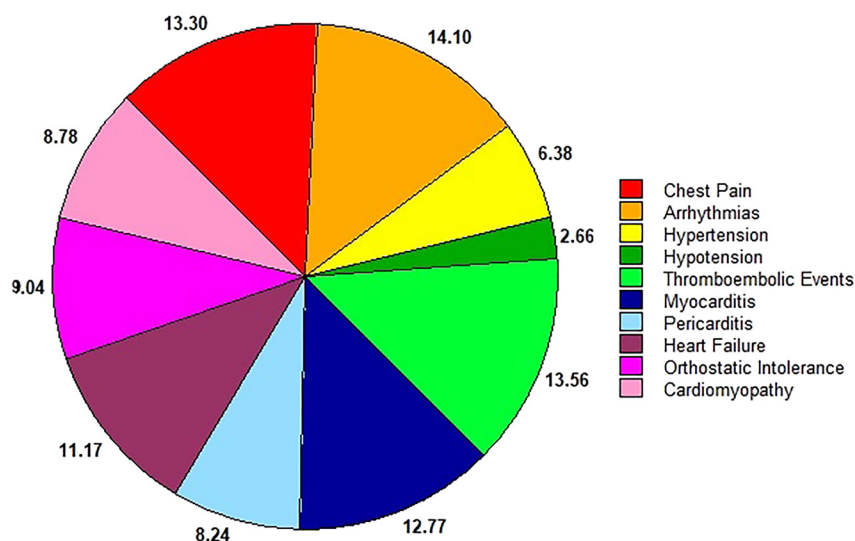


Figure 3: Cardiovascular manifestations of long COVID-19 [4–6, 11, 14–70].

Thromboembolic disease

Thromboembolic disease has been identified as a common sequela of long COVID-19. As a whole, thromboembolic disease was encountered in 51 of the 60 evaluated articles, making up 13.56 % of the total symptomatology. Additionally, an induced hypercoagulable state has been found to be the etiology of various thromboembolic events such as the following: venous thromboembolism (VTE), including deep vein thromboses (30 total articles), and arterial thromboembolism, including cerebrovascular events (31 articles) such as stroke, myocardial infarction/coronary artery disease (CAD, 34 articles), pulmonary embolism (26 articles), and others for a total of 44 articles. This is demonstrated in Supplementary Figure 3.

Discussion

Pathophysiology

It is evident that many COVID-19 survivors have experienced cardiovascular complications after recovery from acute-phase infection. Although there is still a significant gap in our current knowledge and limited randomized control studies to provide statistics, it has been observed that long COVID does not discriminate based on health status. In other words, patients without existing cardiovascular disease, free from comorbidities, and with a low risk of cardiovascular disease prior to initial COVID-19 infection, may also demonstrate symptomatology of long COVID-19 infection. Currently, there is still a paucity of data to elucidate a clear pathophysiology describing the development of long

COVID. Symptoms are suggested to arise secondary to long-term tissue damage during acute infection, ongoing pathological inflammation, cytokine storm, hypoxia, endothelial dysfunction, angiotensin-converting enzyme 2 (ACE-2) downregulation, and/or an exacerbated immune response. Figure 4 demonstrates various proposed pathophysiological etiologies of long COVID-19 and how frequently these theories were encountered in our literature review. Supplementary Table 2 demonstrates etiologies and their corresponding references. Further research is required to establish a better understanding of the pathophysiology and mechanisms responsible for the development of long COVID-19.

A brief summary of current presurgical cardiac recommendations

Given the relative recency of the emergence of this disease, there are currently no standardized recommendations available to guide the presurgical cardiac examination in the context of long COVID-19. Multiple organizations (ACC/AHA [71], European Society of Cardiology/European Society of Anesthesiology [72], Canadian Cardiovascular Society [73], etc.) have suggested detailed presurgical cardiac risk stratification algorithms; however, none of these structures are employed universally. Still, there is a shared responsibility of providers to assess preoperative cardiac fitness in order to decrease the risk for major adverse cardiac events associated with surgical procedures in the setting of long COVID. A recent article from the *Journal of Cardiothoracic and Vascular Anesthesia* states that “Although the data are limited on when it is safe to schedule

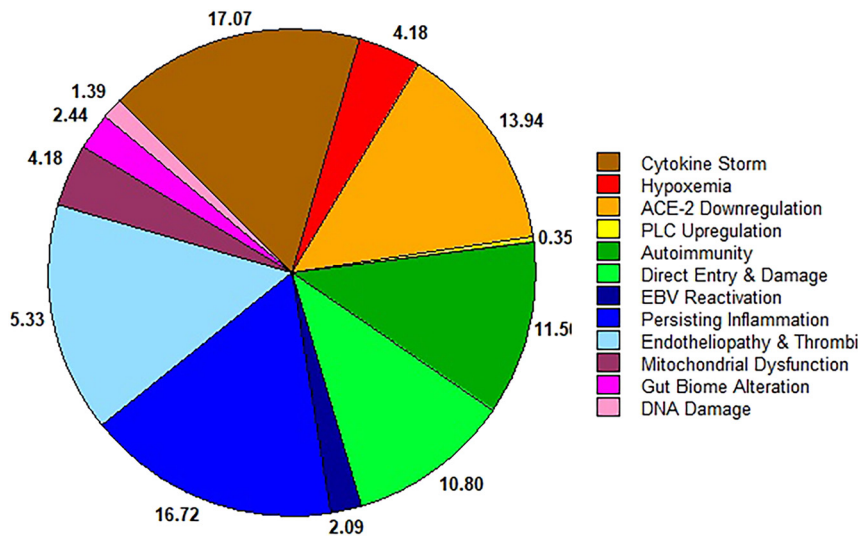


Figure 4: Proposed pathophysiology of long COVID-19 [4–6, 11, 14–70].

an elective surgery after acute infection, patients recovering from COVID-19 are at increased risk of a 30-day adjusted mortality when undergoing elective or emergent surgery,” [5] Additionally, an international, multicenter, prospective cohort study found that the risk of mortality returned to baseline 7 or more weeks after recovering from COVID-19 infection; however, patients with persisting symptoms continued to have increased mortality after 7 weeks [74].

Per the ACC/AHA Task Force on Practice Guidelines, “The preoperative evaluation of the patient undergoing noncardiac surgery can be performed for multiple purposes, including: 1) assessment of perioperative risk (which can be utilized to inform the decision to proceed or the choice of surgery and which includes the patient’s perspective); 2) determination of the need for changes in management; and 3) identification of cardiovascular conditions or risk factors requiring longer-term management” [75].

Perioperative management should be pragmatic, with strict adherence to previously established standards of care [5]. Although preoperative evaluation must take into account patient-specific factors and acuity of the presenting illness, the first step in proposed algorithms is typically a detailed history and physical examination. According to a preoperative cardiac risk article published by the American College of Surgeons [1], “Major perioperative cardiac guidelines all recommend beginning preoperative cardiac risk assessment with a focused history and physical exam to identify unstable or undiagnosed cardiac conditions, estimate the risk of MACE and determine who may benefit from addition testing or revascularization prior to surgery.” Prior to the procedure, cardiac symptoms should not be minimized. Frequently

encountered symptoms such as postacute chest pain and palpitations could indicate a dangerous or significant underlying etiology.

In addition, some guidelines recommend an accompanying ECG +/- measurement of cardiac biomarkers for all patients, whereas some recommend ECG only for those undergoing an intermediate risk to high risk of noncardiac surgery [72]. In conjunction, these initial investigations should be utilized to rule out any potentially serious underlying cardiac disorders, including CAD (e.g., prior myocardial infarction and angina pectoris), HF, symptomatic arrhythmias, history of orthostatic intolerance, and to assess for the presence of a pacemaker or implantable cardiac defibrillator (ICD) [71].

It is also necessary to include measures such as age, comorbidities (e.g., diabetes mellitus, peripheral vascular disease, renal dysfunction, and chronic pulmonary disease), functional capacity (expressed in metabolic equivalent [MET] levels), and type of surgery in cardiac risk evaluation [71]. Cardiac risk stratification as dictated by the ACC/AHA is displayed in Supplementary Table 3.

Based on patient-specific clinical predictors, cardiovascular risk indices, and surgical risk, supplemental testing may be ordered. Supplemental preoperative evaluation may include, but is not limited to, echocardiography, stress testing (exercise or pharmacological), ambulatory ECG monitoring, or coronary angiography. Invasive coronary angiography should be utilized sparingly and reserved for cases in which there is a strong suspicion of obstructive coronary disease or vasospasm [43]. Although it would be impractical to perform cardiac magnetic resonance imaging (CMRI) in all presurgical long-COVID patients, this may be

pursued for patients with cardiac abnormalities suggestive of myocardial scarring or fibrosis. The ACC/AHA has adapted a presurgical cardiac examination specific for those with known CAD or with risk factors for CAD [74]. Further research is required to determine if a history of COVID-19 infection meets the criteria for “CAD risk factors” and automatically places a patient on this path.

Per Khazaal et al., “Even though COVID-19 is linked to a prothrombotic condition, there is presently no consensus on the benefits of VTE prevention in the outpatient environment” [35]. Current guidelines propose anticoagulant therapy for at least 3 months in patients with VTE in the setting of COVID-19 [35].

Across each of these guidelines, a common theme is the need for a multidisciplinary approach that emphasizes communication between the patient, primary care physician, anesthesiologist, surgeon, and outside consultants if deemed necessary [71–73].

Implications for presurgical cardiac examination

As encountered in our literature review, it is evident that long COVID-19 can negatively impact the cardiovascular system and present in many different forms. Table 2 demonstrates examples of the impacts that long COVID may have on various testing modalities encountered in the presurgical cardiac examination. This table is not all-inclusive but serves to provide a baseline representation of the unfavorable cardiac effects of this puzzling disease. An appropriate way of approaching this table would be to consider “Long COVID-19 can cause (insert complication), which would negatively impact (insert evaluation).”

Table 2: How long COVID may impact the presurgical cardiac examination [4, 5, 7, 11, 14–69].

Evaluation	Complications
History and physical examination	– Dull or sharp pain and/or tightness or burning sensation in chest – Palpitations – Shortness of breath – Anxiety Elevated (>140/90 mmHg) or decreased BP (<90/60 mmHg) – Headaches – Vision changes – Dizziness – Confusion – Nausea

Table 2: (continued)

Evaluation	Complications
ECG/ambulatory ECG	– Syncope and falls – S3 gallop – Rales – Edema – Pericardial friction rub – Elevated jugular venous pressure – Pulsus alternans – Postural lightheadedness – Orthostatic hypotension: a drop of 10 mmHg in diastolic BP within 2–5 min of standing – Fatigue – Deep vein thrombosis – Pulmonary embolism – Myocardial infarction – Cerebrovascular event (such as stroke)
	– Tachycardia – Bradycardia – Atrial fibrillation – Atrial flutter – Nonsustained ventricular tachycardia – Premature ventricular contractions – Ventricular fibrillation – AV block – Ischemic changes – Widespread ST-elevation and/or PR-depression
	– ST-segment abnormalities
	– Increased troponin
	– Increased NT-proBNP
	– Increased inflammatory markers
	– Localized wall motion abnormalities (hypokinesia, akinesia, dyskinesia)
	– Diastolic or systolic dysfunction
	– Reduced ejection fraction
	– Thickened and hyperechogenic pericardium
	– Serous, hemorrhagic, or purulent pericardial effusions
	– Ventricular hypertrophy
	– Dilated cardiac chambers
	– Reduced global contractility
	– Mitral regurgitation
	– Cardiac thrombi
	– Coronary artery disease
Stress test (exercise or pharmacological)	– Angina – Arrhythmia – Heart failure – Heart valve disease
	– Cardiomyopathy
	– Coronary artery disease
	– Cardiac thrombi
Coronary angiography	– Coronary artery disease
	– Cardiac thrombi

AV, atrioventricular; BP, blood pressure; ECG, electrocardiogram; NT-proBMP, N-terminal prohormone of brain natriuretic peptide.

Suggestions

As previously mentioned, there are no standardized recommendations available at this time to dictate an approach to presurgical cardiac examination in the context of long COVID-19. The knowledge that is available today leaves clinicians with broad discretion [33]. As such, it is recommended that the preoperative workup should take into account the patient's medical history, including the timing and severity of acute COVID-19 infection, as well as comorbidities and the gravity of the procedure that is anticipated. With these factors in mind, tests should be ordered on a case-by-case basis specific to the circumstances. Physicians should broach each patient case with the intention of ruling out serious cardiovascular comorbidities or complications that may increase the risk for perioperative morbidity and mortality. Additionally, with the paucity of current data, clinicians should have a relatively low threshold to assess postacute COVID-19 patients for cardiovascular morbidity. As emphasized by Kopanczyk et al. [5], the presurgical workup should be pursued with enough time to carry out an appropriate cardiac workup, and deferring presurgical evaluation to the day of surgery should be strongly advised against, with the exception of the urgent or emergent need for surgical intervention. In the setting of an elective procedure, this may include longer-term follow-up to minimize perioperative surgical risk.

Early cardiologist involvement in the setting of persistent cardiovascular symptoms and/or abnormal cardiac test results is recommended. As previously mentioned, post-COVID and presurgical chest pain should not be disregarded and the patient should be investigated for underlying HF, CAD, and arrhythmias. In addition to history, physical examination, ECG, and subsequent indicated testing, a thyroid cascade panel may prove prudent, especially when the patient is experiencing other worrisome symptoms.

Given the established association between long COVID-19 and cardiac dysautonomia, it may be beneficial to obtain a baseline assessment of orthostatic blood pressure and heart rate. Additionally, if warranted, clinicians may consider formal head-up tilt table testing [41] or assessment in an autonomic specialty clinic.

The decision regarding if/when to proceed with surgery should weigh the increased risk of perioperative hazards with the potential threat of delaying the procedure.

Study limitations

Despite the best efforts and research, this review has its limitations. The primary limitation that may bear impact on

the conclusions of this study are the novelty of the COVID-19 and long-COVID disease processes. The scope of this review and thus conclusions drawn from the research is limited by short observation periods.

Additionally, while bibliographic databases have been thoroughly searched for pertinent research studies, not all available registries and literature databases were utilized. As such, it is possible that relevant studies were missed in consideration. Additionally, publications were excluded for the purpose of this review if they were published in a language other than English. This leaves the potential for missed articles published in other languages.

Future studies

Despite increasing public interest in long COVID-19 and its implications in population health, research pertaining to this topic will continue to face significant hurdles. The nature of long COVID, characterized by perseverating symptomatology after the acute phase of infection and lacking a fully elucidated pathophysiologic etiology, may prove burdensome to measure, diagnose, and treat. It is evident that long COVID represents a substantial public health burden. Research priorities for the cardiovascular sequelae of COVID-19 in particular should include elucidating the pathophysiology as well as identifying patient populations that are more vulnerable to cardiovascular long COVID and any corresponding risk factors.

Additionally, it has yet to be determined if post-COVID-19 symptoms could be permanent or not, thus adding to the disease burden. Significant research, including long-term surveillance of COVID-19 survivors even after recovery and discharge, will be required to answer this question and characterize the long-lasting deleterious effects of COVID-19.

With regard to the surgical field, a substantial gap still exists in the current literature and comprehensive understanding of long COVID regarding its multisystemic impacts on presurgical risk stratification. There is a need for the development of applicable presurgical guidelines in particular patient populations, such as those with comorbidities or those with increased risk of specific perioperative complication. Increasing numbers of presurgical candidates with a previous diagnosis of COVID-19 emphasizes the need for continued research and potentially long-term multinational studies exploring the implications of long COVID and its persisting impacts on the general public. Additionally, it would be helpful to explore surgical outcomes in terms of morbidity and mortality in those with a history of COVID-19 infection during a particular timeframe (i.e., within the past 12 weeks, 6 months, etc), in contrast to those who have

not had an infection documented in the same period. Only with continued research will we be able to address the extensive cardiovascular consequences of the COVID-19 pandemic and identify effective therapeutic targets.

Conclusions

In summary, the COVID-19 pandemic has significantly impacted our way of life and has contributed to substantial morbidity and mortality in the acute phase. Acute COVID-19 infection is proposed to be a significant driver for the development of cardiovascular disease and has shown substantial heterogeneity in forms of cardiac involvement. Regardless of whether these effects are secondary to direct myocardial injury, continued inflammation, ACE-2 down-regulation, etc, we are finding more and more patients who are burdened with cardiovascular complications in the postacute setting, thus adding synergistically to the already high burden of cardiovascular morbidity across the globe. There are still many unknowns regarding postacute COVID-19; however, based on current knowledge, we can state that: (1) long COVID does not discriminate which patients it affects by means of acute-phase disease severity or existing comorbidities. Therefore, cardiac conditions associated with long COVID require special attention due to an increased risk of sudden cardiac death, myocarditis, stroke, and myocardial infarction – even in those who were healthy prior to acute COVID-19 infection; (2) long COVID-19 may affect multiple organ systems, including the cardiovascular system; and (3) those patients who develop long COVID-19 are at higher risk of developing long-term cardiac complications than those who do not.

Strategies for evaluating and managing long COVID and its cardiovascular sequelae are evolving in real time; however, there still exists a multitude of opportunities to better illuminate the epidemiology and pathophysiology of the disease as well as to develop guidelines for treatment and targeted therapeutic modalities. We believe that a deeper understanding of the disease process of long COVID is, at this time, prevented by the paucity and limitations of established literature. There is a need for institutions to develop preoperative and risk-specific protocols for postacute COVID-19 patients. Until more specific scientific evidence comes to light, care of these patients should be viewed through the prism of best practices already in use [5], and clinicians should maintain a low threshold to pursue more extensive cardiac workup.

This review serves to add to the growing body of literature exploring the postacute cardiovascular outcomes of COVID-19, with a focus on presurgical cardiac clearance. In organizing these data according to symptoms and their

prevalence throughout the studied literature, we draw attention to the breadth of potential cardiovascular complications secondary to long COVID-19. Although current evidence is scarce in both quality and quantity, it is the goal that this review will highlight the negative impacts of long COVID-19 on cardiovascular health and encourage providers to be cognizant of potential sequelae in the context of the presurgical examination. Additionally, it is our hope that this review will prompt clinicians to remain vigilant for underlying cardiac complications in all surgical candidates who have survived COVID-19 infection.

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