Original Article

COVID-19 and the cardiovascular system: a systematic review of the clinical trial landscape

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Background: At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, China. Due to its high rate of interpersonal transmission the disease rapidly spread in China resulting in an epidemic and subsequently a pandemic with severe impact on social, economic and medical systems globally. Our understanding of the SARS-CoV-2 virus and its effects on the human body continues to evolve as new information becomes available. This paper is an overview of ongoing clinical trials registered with ClinicalTrials.gov on August 3, 2020 to guide future research and clinical practice. Our objective is to do a systematic review of the existing trials registered with ClinicalTrials.gov related to COVID-19 and the cardiovascular (CV) system. The aim of this is to describe the ongoing research in order to guide future practice and evaluate areas of deficiencies.

Methods: We conducted our search on ClinicalTrials.gov (https://clinicaltrials.gov/) on August 3, 2020 and used the key terms "COVID-19" and "cardiovascular. An independent two-person review was carried out for exclusion criteria. Exclusion criteria was defined as studies that were terminated, withdrawn, suspended, of unknown status, or had no connection to the CV system. Three duplicate studies were removed; 141 studies were removed after an independent two person review determined that it did not hold any relevant connection to the CV system and two studies were removed from the data as they were withdrawn and suspended respectively. There were no conflicting opinions between the two researchers regarding the 141 clinical trials excluded. The remaining 122 studies included were then grouped together based on their primary and secondary objectives. The trial was conducted in accordance with the Declaration of Helsinki. No experiments involving humans were done by the researchers and therefore ethical approval was not required.

Results: We found 122 studies applicable to our search criteria and then grouped them together based on topics of investigation as identified by primary and secondary objectives. The identified studies varied from observational, registry based and interventional with most of them falling into the first two categories. The studies were ongoing at that point and did not have results to report or analyze.

Conclusions: Our search on ClinicalTrials.gov produced a variety of studies that investigate relationships between COVID-19 and the CV system. Our search identified the main areas with ongoing research that has the ability to resolve controversies regarding current management of patients with COVID-19 including the ideal thromboprophylaxis regimen; arrhythmogenic potential of patients with COVID-19 and appropriate monitoring of these patients and long term morbidity related to COVID-19 and the CV system. The key finding of our analysis is that the majority of the ongoing studies are observational in nature and not randomized controlled trials. Review of these ongoing studies can aid medical professionals and researchers in outlining current areas of clinical equipoise and help with planning prospective research study topics and design.

Keywords: COVID-19; cardiovascular (CV); cardiology; clinicaltrials.gov; SARS-Cov-2

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Introduction

The spread of the disease known as COVID-19 caused by the novel SARS-CoV-2 viral strain has resulted in a global pandemic. The virus impacts multiple organ systems resulting in a wide variety of clinical presentations. Data on cardiovascular (CV) involvement has been emerging steadily in the literature (1). Specific aspects of interest include risk and benefits of CV specific medications, myocardial injury, ventricular dysfunction, arrhythmias, vascular thrombosis and even the psychological impact of the pandemic on CV health. Multiple clinical trials are underway to study and characterize these areas of interest, and in this paper, we classify these ongoing studies utilizing the ClinicalTrials.gov database. We present the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/jxym-20-110).

Methods

We conducted our search on ClinicalTrials.gov (https://clinicaltrials.gov/) on August 3, 2020 and used the key terms "COVID-19" and "cardiovascular. No filters were applied in order to include all studies registered with the database filtered by the search phrases, regardless of the clinical trial phase or type of clinical trial. An independent two-person review was carried out for exclusion criteria. Exclusion criteria was defined as studies that were terminated, withdrawn, suspended, of unknown status, or had no connection to the CV system. Three duplicate studies were removed; 141 studies were removed after an independent two person review determined that it did not hold any relevant connection to the CV system and two studies were removed from the data as they were withdrawn and suspended respectively. There were no conflicting opinions between the two researchers regarding the 141 clinical trials excluded. The remaining 122 studies included were then grouped together based on their primary and secondary objectives and summarized in Table S1. The trial was conducted in accordance with the Declaration of Helsinki. No experiments involving humans were done by the researchers and therefore ethical approval was not required.

Results

The study search results are shown in *Figure 1*. Based on these search criteria, we identified 268 ongoing clinical trials in the database. We removed 3 duplicate studies and 265 studies remained. After exclusion criteria, 141 studies were subsequently excluded. The specific studies and details of the remaining 122 studies are shown in Table S1. The overview of the studies according to subject area is shown in *Figure 2*. The vast majority of studies focused on anticoagulation or cardiac injury in COVID-19 patients. Observational protocols or registries were the predominant studies.

Discussion

Clinical trials related to the Renin Angiotensin Aldosterone System (RAAS)

Angiotensin converting enzyme inhibitors (ACEi) and Angiotensin Receptor blockers (ARB) are members of a class of widely used medications for hypertension and are favored for their renoprotective effects and impact on CV outcomes. It has been discovered that the SARS-CoV-2 virus enters the lungs through the ACE2 receptor. In animal models, the use of ACEi and ARB led to an increased expression of ACE2 membrane bound aminopeptidase in the pulmonary, CV and renal systems (2,3). Thus, some healthcare providers and media sources have questioned the continued use of ACE inhibitors and ARBs due to concerns that patients could experience an augmentation of SARS-CoV-2 infection and severity due to these drugs (4). In contrast, emerging research suggests that the use of these drugs is likely safe in COVID-19 (5). Some research even suggests that RAAS blockade has potential benefits in the prevention and treatment of lung injury caused by COVID-19 (6,7). The current recommendation from the European Society of Hypertension, the European

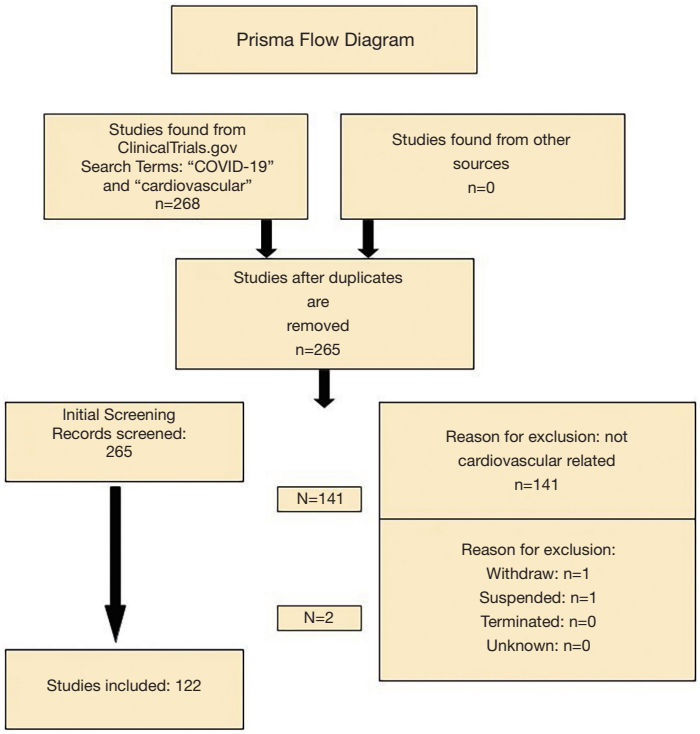

Figure 1 PRISMA flow diagram.

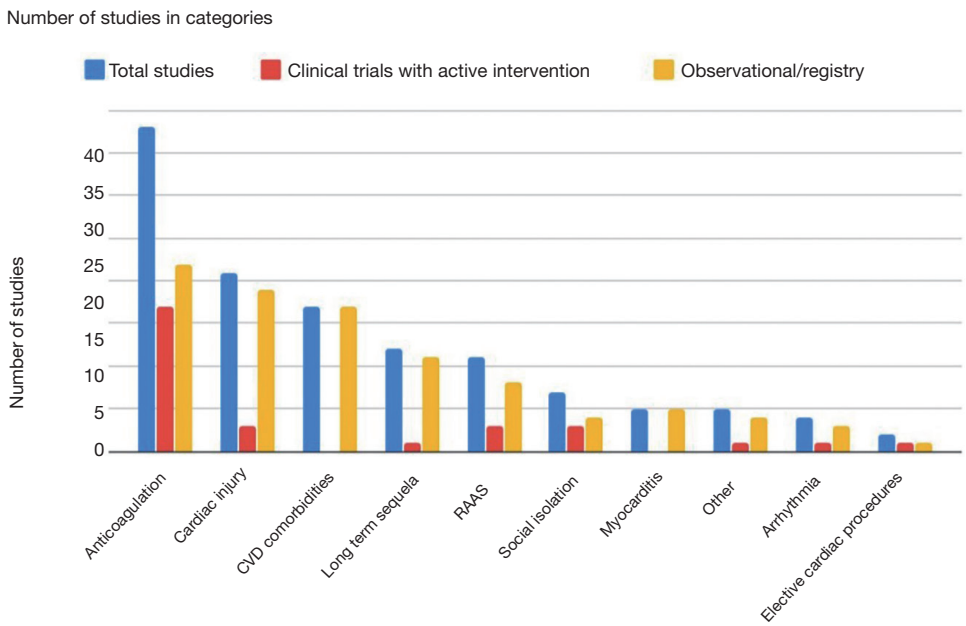

Figure 2 Chart representing the number of studies within each category.

Society of Cardiology, the American Heart Association, the Heart Failure Society of America, and the American College of Cardiology is not to withhold RAAS blockers as a standard of therapy (8,9). Much of the currently published data consists of animal studies or expert opinions and therefore high quality research is needed to better understand the interaction of COVID-19 and RAAS.

In our search of ClinicalTrials.gov, we found 11 studies investigating the correlation between RAAS and COVID-19 disease course, 3 of which are interventional randomized controlled clinical trials (RCTs) while the remaining are large volume observational studies (Table S1, studies 1–11). Combined, the observational studies are targeting 11,155 participants with the largest observational study having 7,000 recruits. This latter study (Mach *et al.*, study #8 in Table S1) is a single center observational study at the Geneva University Hospital whose primary aim is to gather data comparing clinical outcomes in COVID-19 hospitalized patients with and without CVD. Furthermore, the investigators will study prognosis and outcomes according to the use of RAAS blockade. Other studies in this category compare time to clinical improvement, severity of disease, and mortality in patients using versus not using RAAS blockade. The 3 interventional studies (Montalescot *et al.*, study #4, Lopes *et al.*, study #5, and University of Pennsylvania, study #7 in Table S1) all test continuation versus discontinuation of RAAS blockers in patients admitted with COVID-19 infection previously using these medications, and will enroll a total of 1,406 participants. Primary objectives of these studies include (I) time to clinical improvement, (II) number of days alive in and out of the hospital, and (III) composite endpoint including time to death, number of days requiring mechanical ventilation or extra-corporeal membrane oxygenation (ECMO), number of days requiring renal replacement therapy or vasopressor use, and Sequential Organ Failure Assessment (SOFA) scores.

Anticoagulation and prothrombotic state in COVID-19 patients

Evidence of abnormal coagulation parameters associated with COVID-19 appeared in early reports from China and Japan (10). A prominent increase in D-dimer levels as a predictor of adverse outcomes is persistently seen in COVID-19 infection suggesting an underlying coagulopathy (11). Based on this observation, ongoing studies aim to understand the prevalence and characteristics of coagulation abnormalities in these patients while others investigate therapeutic options. Our search revealed a total of 38 studies that investigate the relationship between anticoagulation and COVID-19 (Table S1, Studies 12–49). Twenty-two of these studies are observational in nature, while 16 test an intervention. Many of the studies aim to determine which anticoagulation regimen is beneficial and safe, while others aim to describe the incidence of thromboembolic complications in COVID-19. The studies are separated into two main objectives: to define the abnormal coagulation parameters identified in COVID-19 patients by means of laboratory testing or to identify the number of thrombotic related complications including deep venous thrombi (DVT), pulmonary emboli (PE), and arterial thrombi. Thirteen of the interventional studies compare the standard of care thromboprophylaxis to an intervention for prevention of thrombotic events. These latter studies assessed the outcomes for efficiency of the intervention at preventing thrombotic complications and the safety in terms of bleeding risk. The interventional drugs include therapeutic anticoagulation with low molecular weight heparin (LMWH), unfractionated heparin, direct oral anticoagulants (DOACs), and adjusted dose prophylaxis with LMWH. One interventional trial investigates whether infusion of an Angiotensin 1–7 related peptide is effective at normalizing the hypercoagulable state (Owen *et al.*, study #39 in Table S1). The authors hypothesize that the coagulopathy associated with COVID-19 is driven by overactivation of the RAAS system causing a relative deficiency of Angiotensin 1–7 peptide (12).

Arrhythmias

A heightened concern for increased arrhythmic burden (atrial and ventricular) has been present in patients with COVID-19. Recently, a meta-analysis stated that 19% of hospitalized patients and 48% of patients in the Intensive Care Unit with COVID-19 and poor outcomes had cardiac arrhythmias (13). Cardiac arrhythmias, hypotension and sudden cardiac death are each associated with COVID-19 (14). Cardiac injury by biomarker detection or frank ventricular dysfunction in these patients is also associated with the development of arrhythmias. Our search revealed 4 studies concerning COVID-19 and cardiac arrhythmias (Table S1, studies 50–53). Out of these 4 studies, 1 was an interventional clinical trial and 3 were observational. Although only 4 studies were identified, the observational studies

combined include 21,000 targeted recruits. The COVIDAR Registry (Arbelo *et al.*, study #52 in Table S1) is an international longitudinal multicenter observational study which aims to assess the incidence, type, and risk factors of arrhythmias in the context of SARS-CoV-2 infection, while also providing relevant information on events and major CV outcomes. The primary objective is to describe the time from the onset of first arrhythmia to 12 months post admission or death. All 3 of the observational studies aim to characterize the arrhythmia burden in COVID-19 patients. Improved characterization of arrhythmia burden and mechanism of death is critical in guiding the need for developing treatment strategies as some of the current pharmacological therapies (hydroxychloroquine, azithromycin) have arrhythmogenic potential (15). To this end, one specific trial (Reddy *et al.*, study #53 in Table S1) is studying remote cardiac monitoring with a VitalConnect Vital Sign Patch (VitalConnect, San Jose, CA) for patients with COVID-19 managed in the outpatient setting to characterize arrhythmia burden.

The effect of CV comorbidities on COVID-19 infection

Observations from early in the pandemic demonstrated that patients with baseline cardiometabolic comorbidities were at a higher risk of suffering a severe form of COVID-19 infection. A study of 44,672 patients with COVID-19 found that a history of CVD was associated with a nearly five-fold increase in the case fatality rate when compared to patients without CVD (10.5% *vs.* 2.3%) (16). In addition, multiple publications now have linked CVD risk factors such as age, diabetes, obesity and hypertension with poor outcomes in COVID-19 (17,18). The present search identified 17 clinical trials investigating the association between COVID-19 infection and the severity of disease based on the presence of CV comorbid conditions (Table S1, studies 54–70). All the trials are observational by design. They investigate whether comorbid CV conditions translate into a higher risk of severe infection, higher mortality rates, and increased morbidity post recovery at certain time intervals. Combined, these trials have 52,907 recruits. The largest of the observational trials is a Swedish nationwide registry based case control study (Karolinska Institute, study #66 in Table S1) that has an estimated enrollment of 22,784 participants with an aim to study risk factors and the effect they have on outcomes for severe COVID-19, with a focus on CVD, different treatments, and socioeconomic factors. Similarly, another study in France (Weizman *et al.*, study #63 in Table S1) with 2,878 participants aims to identify early predictors of clinical worsening in patients hospitalized for COVID-19. Clinical data relating to history, comorbidities, risk factors, treatments, clinical parameters, biological and cardiological data, procedures and events during hospitalization will be recorded. A Spanish study (Torres *et al.*, study #62 in Table S1) aims to characterize the effect that comorbid CV conditions have on long term (one year) outcomes of patients admitted to the hospital with severe COVID-19. One study (Parati *et al.*, study #68 in Table S1) uses artificial intelligence to create a risk scoring system taking into account various clinical and laboratory findings to predict in-hospital outcomes. Lastly, a global observational study from the World Heart Federation (Silwa *et al.*, study #70 in Table S1) utilizes a survey method to better understand specific conditions that increase the risk of developing severe COVID-19 and to better characterize CV complications in hospitalized patients. Considering the high global prevalence of CVD and its suggested link with COVID-19, it is imperative that robust studies be conducted to further investigate these issues.

Myocarditis and cardiac injury in COVID-19

Cardiac injury has been documented in the earliest COVID-19 patients in Wuhan, China. A number of COVID-19 related myocarditis cases have been reported (19,20). The pathophysiology of COVID-19-related myocarditis is thought to be a combination of direct viral injury and cardiac damage due to the host's immune response. The prevalence of myocarditis among COVID-19 patients is unclear, partly because the early reports often lacked the specific diagnostic modalities to assess myocarditis (21). Fulminant myocarditis has been described in the literature and due to its aggressive course and high mortality, physicians should maintain a high index of suspicion. One study suggests that up to 7% of deaths in COVID-19 might be due to myocarditis but further research is needed (22).

We identified 5 ongoing clinical trials of observational design with the aim to better define the relationship between COVID-19 infection and myocarditis. All five studies use biomarkers and/or imaging to evaluate patients (Table S1, studies 71–75). One study (Minville *et al.*, study #73 in Table S1) plans to use multiple imaging modalities to not only diagnose COVID-19 myocarditis but follow the patients daily to determine the evolution of

their functional myocardial parameters during the acute infection. One study (Berry *et al.*, study #71 in Table S1) of prospective, observational, multicenter, longitudinal cohort design will use advanced CV imaging to identify the proportion of patients with myocardial inflammation that is sub-clinical or clinically overt. The investigators will identify patients upon admission to the hospital with broad inclusion criteria (>18 years old hospitalized with COVID-19) and perform imaging with cardiac magnetic resonance imaging (MRI) at 28 days post discharge to identify myocardial inflammation which will be classified using the Lake Louise criteria (23). Furthermore, one of the studies (Delmas *et al.*, study #72 in Table S1) investigates the clinical characteristics of SARS-CoV-2 myocarditis by using clinical, biological (troponin and proBNP), and imaging presentations to correlate with patient outcomes over 6 months post discharge.

Apart from myocarditis, there has been an interest in the impact of COVID-19 on major adverse cardiac events (MACE) and on myocardial injury—most often defined as elevation of troponin levels. Ongoing clinical trials attempted to quantify the incidence of myocardial injury and MACE in patients with COVID-19. The researchers use multiple modalities, including imaging, clinical observations and biochemical data to better describe the exact nature of cardiac injury. Other interventional trials study various drugs (including statins and colchicine) to evaluate their potential cardioprotective effects. Our search revealed 21 studies that discussed the relationship between cardiac injury and COVID-19 (Table S1, studies 76–96). Of these studies, 18 are observational and three are interventional. Interventions tested include aspirin, clopidogrel, atorvastatin, rivaroxaban and colchicine. The aim of the interventions is to assess if any will alter the natural course of the disease and provide CV protection in SARS-CoV-2 infected patients.

Of the 18 observational studies, 3 studies investigate the incidence of acute coronary syndrome (ACS) in the presence of COVID-19 while 6 studies characterize the incidence of MACE. One of the studies (Hao *et al.*, study #83 in Table S1), in China, specifically looks at whether anxiety related to the pandemic increases the incidence of ACS. One study (Tarkin *et al.*, study #96 in Table S1) identifies disease-specific patterns of myocardial injury in COVID-19 using non-invasive multi-modality cardiac imaging paired with cytokine/chemokine testing, immunophenotyping of peripheral blood cells, and coagulation profiles. The aim is to classify injury patterns based on immune cell profiles. Another study (Papa *et al.*, study #85 in Table S1) plans to perform postmortem autopsies on the hearts of patients who died due to COVID-19. The primary objective is to understand the pathology and pathogenesis of cardiac injury in patients with COVID-19—with and without CV comorbidities. Three studies use transthoracic echocardiographic imaging to detect and classify the cardiac injury in patients with COVID-19. Four of the studies evaluated biomarkers of injury and stress such as troponin and proBNP.

Long term CV sequelae

The long term pulmonary and cardiac sequela of patients who recovered from COVID-19 pneumonia is unknown. As more is revealed about acute mortality in COVID-19, experts are becoming more concerned with the future morbidity that these patients will experience. Our search produced 12 studies concerning this topic (Table S1, studies 97–108). Seven of these studies were observational, while only one was interventional. Two studies (Monnet *et al.*, study #108 and Katz *et al.*, study #99 in Table S1) investigate the incidence of left ventricular dysfunction development and elevation of proBNP post COVID-19. One study (Katz *et al.*, study #97 in Table S1) aims to investigate the incidence of decline in ejection fraction (EF) >10% at 30 days post discharge. Two other studies (Ortega Paz *et al.*, study #98 and study #107 from Uppsala University in Table S1) investigate CV mortality at 1-year post COVID infection. Other researchers are examining the effect on cardiac electrophysiology and plan to follow COVID-19 survivors with serial ECGs. (University of Hong Kong, Study #102, Table S1). The remaining observational studies are less specific, casting a broader net as to the possible CV sequelae following SARS-Cov-2 infection.

Effect of COVID-19 on elective cardiac procedures

COVID-19 has caused disruptions in scheduled invasive procedures and required triage of patients awaiting CVD treatment (24,25). Our search presented 2 studies that delve into this topic, one of which was interventional and the other observational (Table S1, studies 109–110). One study (Pilgrim *et al.*, study #110 in Table S1) is investigating the effect of the pandemic on deferral of valvular replacement in patients with severe aortic stenosis on morbidity and mortality while an interventional study (Nia *et al.*, study #109 in Table S1) provides digital cardiac counselling to

patients awaiting cardiac procedures to assess its effect on mortality and MACE.

Effect of social isolation

Due to the highly infectious nature and rate of spread of SARS-CoV-2, the global community largely determined that social isolation was necessary to curb exponential spread that threatened to overwhelm the healthcare system (26). Social isolation further functions as a tool to flatten the infection rate curve and thus protect those at a higher risk of attaining the disease. Conversely, others fear that due to a decrease in physical activity levels during this social isolation, decompensation of CV comorbid conditions might occur (27). We identified several studies investigating the effect of social isolation on CV comorbidities. Our search displayed seven studies that assessed the effect of social isolation on CV health (Table S1, studies 111–117). Four of these studies were observational and the remaining three were interventional.

One study (Berard *et al.*, study #111 in Table S1) utilizes telephonic interviews at various intervals to assess compliance to medication, exercise routine and diet during quarantine. This study also measures anxiety levels due to social isolation and will see if that affects adherence to lifestyle changes. One large observational study (Centre Hospitalier Universitaire Dijon, study #112 in Table S1) investigates medication compliance during social isolation while another (Brunner *et al.*, study #113 in Table S1) assesses changes in physical activity during the quarantine. We furthermore identified interventional trials investigating the success of digital telemedicine platforms providing advice and counselling regarding compliance and telerehabilitation done by a physiotherapist (Kortianou *et al.*, study #115 in Table S1) during this period of social isolation. The large randomized interventional trial (study #116 done at the University Hospital, Tours; Table S1) called CONQUEST investigates whether a phone call made by a general practitioner and medical student is successful at identifying patients at risk of decompensation from their chronic condition and if this approach is able to prevent hospitalization. Another interventional study (Burlacu *et al.*, study #114 in Table S1) investigates an electronic platform to assist patients with counseling regarding chronic CV conditions given their inability to attend routine follow up visits in the clinic.

Other relevant studies

Our search also produced 5 studies that did not fit within the above criteria (Table S1, studies 118–122). These studies looked at a variety of different concepts, including technology assistance in patient risk stratification for CV interventional procedures, the evolution of psychosocial, CV, and immune markers in healthcare professionals to assess the effects of pandemic work burden, statin therapies, and treatment and outcomes for ST segment elevation myocardial infarction (STEMI) care with primary percutaneous coronary intervention during the pandemic. Four of these studies are observational and one is interventional. The one observational study (Masana *et al.*, study #121 in Table S1) investigates whether simvastatin therapy interferes with some of the inflammatory pathways activated by COVID-19 to produce the cytokine storm responsible for ARDS. The primary outcome compares the clinical course and prognosis of patients on statin therapy to statin-naive patients. A large retrospective multicenter registry study (Università degli Studi del Piemonte Orientale "Amedeo Avogadro", study #122 in Table S1) aims to estimate the real impact of COVID-19 pandemic on treatment and outcome of STEMI by primary angioplasty, and to identify risk factors for delay or deferral in seeking treatment.

Limitations

Our trial review was limited in that full trial data is not available for any of the clinical trials. Furthermore, we did not include clinical trials that were not registered with ClinicalTrials.gov and therefore could be missing key clinical trials. Another limitation is the dynamic nature of COVID-19 research with new trials registered on a daily basis with ClinicalTrials.gov. This means that an update to this systematic review might be useful in the future to include new trials registered and review the data available from completed trials in our review that is currently not available.

Conclusions

Our search on ClinicalTrials.gov produced a variety of studies that investigate relationships between COVID-19 and the CV system. Our search identified the main areas with ongoing research that has the ability to resolve

controversies regarding current management of patients with COVID-19 including the ideal thromboprophylaxis regimen, arrhythmogenic potential of patients with COVID-19 and appropriate monitoring of these patients and long term morbidity related to COVID-19 and the CV system. The key finding of our analysis is that the majority of the ongoing studies are observational in nature and not randomized controlled trials. Review of these ongoing studies can aid medical professionals and researchers in outlining current areas of clinical equipoise and help with planning future prospective research study topics and design.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at http://dx.doi.org/10.21037/jxym-20-110

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jxym-20-110). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Characterization of included studies from ClinicalTrials.gov

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
RAAS related studies						
1	ARB, ACEi, DRi Usage in COVID-19/Ivanov *et al.*/ NCT04364984	Recruiting	Observational (patient registry)	10	The entry of COVID-19 using ACE receptors has led to many theories on the effect ACEi has on risks for infection and severity of infection.	Primary outcome: -BP (hypertensive efficacy) (time frame: 4 weeks) Secondary outcome: -COVID-19 course (time frame: 3 weeks)
2	Phase IV Observational Study to Associate Hypertension and Hypertension Treatment to COVID19/Muiesan *et al.*/ NCT04331574	Recruiting	Observational (patient registry)	2,000	This study aims to verify whether the chronic intake of RAS inhibitors modifies the prevalence and severity of the clinical manifestation of COVID-19.	Primary outcome: -Number of COVID-19 patients admitted who used ACE/ARB (time frame: 3 months) -Number of COVID-19 patients admitted that did not used ACE/ARB
3	Prospective Monitoring of Drug Safety and the Occurrence of Complications During Hospitalization in Patients With Cardiovascular Diseases With COVID-19/Januszewicz *et al.*/ NCT04374110	Recruiting	Observational (patient registry)	1,000	This study aims to assess the safety of the cardiovascular drugs in relation to the occurrence of complications during hospitalization in patients with CVD and COVID-19 infection.	Primary outcome: -Adverse events (time frame: 2 weeks) -Death, myocardial infarction, heart failure, myocarditis, acute renal failure, stroke
4	ACE Inhibitors or ARBs Discontinuation for Clinical Outcome Risk Reduction in Patients Hospitalized for the Endemic Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) Infection: the Randomized ACORES-2 Study/Montalescot *et al.*/NCT04329195	Recruiting	Interventional (clinical trial): intervention tested: discontinuation vs continuation of RAS blocker therapy	554	This study aims to assist in addressing whether RAAS blockade should be continued or discontinued in COVID-19.	Primary outcome: -Time to clinical improvement from day 0 to day 28 (improvement of two points on a seven-category ordinal scale, or live discharge from the hospital, whichever comes first) (time frame: from day 0 to day 28 or hospital discharge)
5	Suspension of Angiotensin Receptor Blockers and Angiotensin-converting Enzyme Inhibitors and Adverse Outcomes in Hospitalized Patients With Coronavirus Infection (COVID-19). A Randomized Trial/Lopes *et al.*/NCT04364893	Recruiting	Interventional (clinical trial): intervention tested: suspension or maintenance of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors	700	This study aims to assist in addressing whether RAAS blockade should be continued or discontinued in COVID-19.	Primary outcome: -Median days alive and out of the hospital (time frame: 30 days) Secondary outcome: -Number of participants with adverse cardiovascular outcomes and new worsening heart failure -Cardiovascular biomarkers related to COVID-19
6	Hypertension in Patients Hospitalized With COVID-19 in Wuhan, China: A Single-Center Retrospective Observational Study/Zen *et al.*/NCT04318301	Completed	Observational	275	This study aims to investigate and compare the demographic characteristics, coexisting disease, severity of pneumonia, and the effect of antihypertensive drugs in patients with COVID-19 and hypertension. They specifically aim to assess the effect of ACEi use on COVID-19 pneumonia outcomes.	Primary outcome: -Rate of death (time frame: from date of admission until the date of death from any cause, up to 60 days) -mortality in 28-day Secondary outcome: -Severity of pneumonia -Length of hospital stay
7	The Randomized Elimination or Prolongation of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers in Coronavirus Disease 2019/Chirinos *et al.*/NCT04338009	Enrolling by invitation	Interventional (clinical trial): intervention tested: continuation vs discontinuation of ARB/ACEI	152	This study aims to assist in addressing whether RAAS blockade should be continued or discontinued in COVID-19.	Primary outcome: -Hierarchical composite endpoint (time frame: Up to 28 days) The primary endpoint of the trial will be a global rank score that ranks patient outcomes according to four factors: (I) time to death, (II) the number of days supported by invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO), (III) the number of days supported by renal replacement therapy or pressor/inotropic therapy, and (IV) a modified sequential Organ Failure Assessment (SOFA) score. The modified SOFA score will include the cardiac, respiratory, renal and coagulation domains of the SOFA score.

Table S1(*continued*)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
8	Retrospective Observational Study to Compare the Short, Mid- and Long-term Prognosis and Outcomes of SARS-CoV-2 Infected Hospitalized Patients With Cardiovascular Disease (CVD) to SARS-CoV-2 Infected Hospitalized Patients Without CVD: The Geneva Covid-19 CVD Study/Mach *et al.*/NCT04384029	Active, not recruiting	Observational	7,000	This study aims to gather observational data to compare clinical outcomes in COVID+ hospitalized patients with pre-existing or newly onset cardiovascular disease. The investigators will study prognosis and outcomes according to the patients' medications in the setting of controversy surrounding ACEi/ARB. This will assist in determining the association between COVID-19 disease and CVD, based on age, previous CV diseases, CV risk factors, CV medications (e.g., ACE inhibitors or angiotensin II receptor antagonists)	Primary outcome: -Morbidity of COVID-19 in patients with and without CVS disease (time frame: 0 days, 30 days, 1 year after hospitalization) -Mortality difference between COVID-19 positive patients with and those without CVS disease
9	COVID-19 Blood Pressure Endothelium Interaction Study/NHS Greater Glasgow and Clyde/NCT04409847	Not yet recruiting	Observational	70	The aim of this study is to understand the interaction of COVID-19 on blood pressure responses.	Primary outcome: -ABPM systolic blood pressure (time frame: 24 hours (all day and night)) Secondary outcome: -24 hour, day, night DBP and SBP, dipping status, morning surge, 24 hour, day, night ABPM HR
10	Association Between Hypertension, Renin-Angiotensin-Aldosterone System Inhibitors and COVID-19/Georges *et al.*/NCT04374695	Not yet recruiting	Observational	700	The aim of this study is to analyze the associations between COVID-19 and hypertension, and treatments with ACEi and ARBS.	Primary outcome: -Prior treatment by ACEi (time frame: at admission to hospital) -Prior treatment by ARB Secondary outcome: -Baseline characteristics and comorbidities -Major clinical adverse events
11	Impact of Previous Treatment With Angiotensin II Receptor Blockers in Patients With SARS-Cov2 Infection Admitted to the Intensive Care Unit on Survival and Severity of the Disease (COVID-ARA2)/Asfar *et al.*/NCT04337190	Recruiting	Observational	100	The aim of this prospective study is to determine ACE2 level and activity in patients with SARSCoV2 infection admitted to the intensive care unit (ICU). The study involves serial blood collection for measurement of ACE2 levels.	Primary outcome: -ACE activity over time (time frame: at the day of admission, day 3 and day 7) Secondary outcome: -ACE activity over time -Mortality at 28 days -ARDS severity
Anticoagulation related studies						
12	Analysis of the Coagulopathy Developed by COVID-19 Infected Patients: Thrombin Generation Potential in COVID-19 Infected Patients/Gris *et al.*/NCT04356950	Recruiting	Observational	175	COVID-19 produces a hypercoagulable state that is not well understood yet. Existing coagulation tests like PT/PTT only reflect a small portion of total thrombin generation. The aim is to apply a normalized and automated thrombin generation test (TGT), developed for testing the thrombotic risk (triggered by 5 pM Tissue Factor, with a purified thrombomodulin (TM) challenge) and to study its prediction of survival.	Primary outcome: -28 day survival (time frame: 1 month) -Absolute thrombin generation test latent period -Relative thrombin generation test latent period -Various other coagulation parameters Secondary outcome: -3 month survival rate
13	Coagulopathy Associated With Coronavirus disease19 (CA-COVID19) A Multi-Centre Observational Study in UK/Arachchillage *et al.*/NCT04405232	Recruiting	Observational	5000	Based on Chinese data, abnormal coagulation parameters (Prolonged Prothrombin time (PT) and raised D dimer) are reported to predict a poor prognosis and may therefore be important therapeutic targets. High rates of DVT and PE are also reported in early data. A better understanding of this could aid in AC management.	Primary outcome: -Prevalence and characteristics of coagulation abnormalities and their predictive value for respiratory failure requiring ventilation, multiorgan failure and death in patients presenting with COVID-19 infection (time frame: 12 months)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
14	Coagulopathy of COVID-19: A Pragmatic Randomized Controlled Trial of Therapeutic Anticoagulation Versus Standard Care as a Rapid Response to the COVID-19 Pandemic (RAPID COVID COAG)/Sholzberg *et al.*/NCT04362085	Recruiting	Interventional (clinical study): intervention tested - therapeutic anticoagulation	462	COVID-19 coagulopathy is characterized by elevated D-dimer, an indicator of fibrin formation, and clot lysis, and a mildly prolonged prothrombin time, suggestive of coagulation consumption. This trial compares therapeutic anticoagulation compared to standard care in hospitalized patients with COVID-19 and an elevated D-dimer (≥2X upper limit of normal {ULN}).	Primary outcome: -ICU admission, non-invasive positive pressure ventilation, invasive mechanical ventilation, or all-cause death up to 28 days (time frame: up to 28 days)
15	COVID-19-associated Coagulopathy: Safety and Efficacy of Prophylactic Anticoagulation Therapy in Hospitalized Adults With COVID-19/Perepu *et al.*/NCT04360824	Recruiting	Interventional (clinical trial): intervention tested: standard prophylactic dose enoxaparin vs intermediate prophylactic dose enoxaparin	170	This is a prospective, randomized, open-label, multi-center interventional study designed to compare the safety and efficacy of two LMWH dosing protocols in COVID-19 admissions with modified ISTH Overt DIC criteria score ≥3.	Primary outcome: -Mortality (time frame: 30 Days post intervention) -Risk of all-cause mortality Secondary outcome: -Major bleeding -Arterial thrombosis -Venous thromboembolism
16	Effectiveness of Weight-adjusted Prophylactic Low Molecular Weight Heparin Doses Compared With Lower Fixed Prophylactic Doses to Prevent Venous Thromboembolism in COVID-2019. The Multicenter Randomized Controlled Open-label Trial COVI-DOSE/Zuily *et al.*/NCT04373707	Recruiting	Interventional (clinical trial): intervention tested: weight adjusted prophylactic dose enoxaparin	602	Worldwide observational studies indicate a significant prothrombogenic effect associated with SARS-CoV-2 infection with a high incidence of venous thromboembolism (VTE), notably life-threatening pulmonary embolism. The optimal dose of AC has not yet been determined.	Primary outcome: -Venous thromboembolism (time frame: 28 days) -Risk of deep vein thrombosis or pulmonary embolism or venous thromboembolism-related death Secondary outcome: -Major bleeding -Clinically relevant non-major bleeding
17	Evaluation of TEM-tPA (Thromboelastometry With tPA) to Detect Covid-19 Patients at High Risk of Thrombosis /Hospices Civils de Lyon/NCT04366778	Recruiting	Observational	325	Some patients develop severe thrombotic complications, such as pulmonary embolism, despite anti-thrombotic prophylaxis by low molecular weight heparin. The aim of this project is to evaluate modified thromboelastometry for identifying patients at high risk of thrombosis.	Primary outcome: -Coagulability (time frame: day 0, 3, 6, 9, 12, 15) -Venous thrombotic event (VTE) or arterial thrombosis (time frame: day 15)
18	High Prevalence of Deep Venous Thrombosis in Non-severe COVID-19 Patients Hospitalized for a Neurovascular Pathology/University Hospital, Strasbourg, France/NCT04452422	Recruiting	Observational	30	Severe SARS-CoV-2 infection, responsible of COVID-19, is accompanied by many venous thromboembolic events. Using bedside Doppler ultrasonography (DUS) of lower limbs, this study investigated the rates of DVT in these patients in stroke unit.	Primary outcome: -Number of cumulated deep venous thrombosis among hospitalization (time frame: Day 7 after admission)
19	Incidence of Acute Pulmonary Embolism in Covid-19 Patients on CT Angiography and Relationship to D-dimer Levels/University Hospital, Strasbourg, France/NCT04373486	Recruiting	Observational	160	It has been suggested an independent association between the severity of the disease and the level of D-dimer. Finally, Tang *et al.* showed that anticoagulant therapy is associated with a decreased mortality at Day-28 in severe Covid-19 patients, in favor of a possible associated coagulopathy. The purpose of this study is to describe the rate of pulmonary embolus in patients classified as COVID-19 infection and who underwent chest CT angiography.	Primary outcome: -Rate of positivity for acute pulmonary embolism (time frame: March 1, 2020- March 31, 2020)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
20	Incidence of Thromboembolic Events and Prognosis of COVID-19 Patients Hospitalized in Intensive Care Units in France/University Hospital, Strasbourg, France/ NCT04405869	Recruiting	Observational	300	The main objective of this study is to describe the incidence of thromboembolic events in a population of patients hospitalized in ICUs in France for severe COVID-19. They further evaluate the influence of different anticoagulation regimens on these coagulation parameters and on the incidence of thromboembolic events	Primary outcome: -Analysis of incidence of thromboembolic events in patients with Sars-CoV-2 (time frame: 1 month)
21	Intermediate or Prophylactic-Dose Anticoagulation for Venous or Arterial Thromboembolism in Severe COVID-19: A Cluster Based Randomized Selection Trial (IMPROVE-COVID)/Kirtane *et al.*/NCT04367831	Recruiting	Interventional (clinical trial): intervention tested: heparin and enoxaparin doses for venous or arterial thromboembolism	100	This study assesses the effectiveness of intermediate versus prophylactic doses of anticoagulation in patients critically ill with COVID-19 in the ICUs throughout the hospital. Anticoagulation is part of the patient's usual standard of care but determining the dose of anticoagulation is based on physician preference. The investigators are conducting this study (a randomized trial with adaptive design employing cluster randomization) with the support of all of the ICUs to collect data in order to determine what should be the standard of care in terms of anticoagulation in these critically ill patients.	Primary outcome: -Total Number of Patients with Clinically Relevant Venous or Arterial Thrombotic Events in ICU (time frame: Discharge from ICU or 30 days)
22	Preventing COVID-19-associated Thrombosis, Coagulopathy and Mortality With Low- and High-dose Anticoagulation: a Randomized, Open-label Clinical Trial/ Blondon *et al.*/NCT04345848	Recruiting	Interventional (clinical trial): intervention tested: two different doses of enoxaparin	200	The investigators hypothesize that high-dose anticoagulants, compared with low-dose anticoagulants, lower the risk of venous and arterial thrombosis, disseminated intravascular coagulation (DIC) and mortality. This open-label controlled trial will randomize hospitalized adults with severe COVID-19 infection to therapeutic anticoagulation vs. thromboprophylaxis during the hospital stay.	Primary outcome: -Composite outcome of arterial or venous thrombosis, disseminated intravascular coagulation and all-cause mortality (time frame: 30 days) Secondary outcome: -Arterial thrombosis -Venous thromboembolism -Disseminated intravascular coagulation -All-cause mortality
23	Screening of Cardiovascular Complications in Patients With COVID-19/Doyen *et al.*/NCT04335162	Recruiting	Observational	100	Patients with COVID-19 in the ICU or hospitalized with a severe form have a poor prognosis. High levels of D-Dimers (81% of non survivors) and fibrin degradation products are associated with increased risk of mortality suggesting the possibility of venous thromboembolism.	Primary outcome: -Determine the incidence of cardiomyopathies and venous thromboembolism (time frame: 28 days) Secondary outcome: -Mortality -Duration of mechanical ventilation -Shock at day 28 -Length of stay in the ICU
24	Study of the Prevalence of Deep Vein Thrombosis in Patients Hospitalized in Intensive Care for Acute Respiratory Failure Linked to Pneumonia Documented With SARS-COV2/ Générale de Santé/NCT04388657	Recruiting	Observational	100	Hemostasis abnormalities have been shown to be associated with a poor prognosis in these patients with COVID-19 pneumonia and higher rates of DVT's have been described. This research is based on the hypothesis that the existence of deep vein thrombosis (DVT) could make it possible to screen patients at risk of pulmonary embolism and to set up a curative anticoagulation.	Primary outcome: -Percentage of patients with one or more DVTs (time frame: 28 days)

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Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
25	Thrombo Embolic Events in Critical Care Patients With Covid-19 Serious Acute Pneumopathy/Centre Hospitalier Universitaire, Amiens/NCT04366752	Recruiting	Observational	100	The understanding of hemostasis and inflammation crosstalk has gained considerable knowledge during the past decade in the field of arterial and venous thrombosis.Patients with infection of COVID-19 and severe pneumoniae seem to have higher risk of thromboembolism. Not much data is available regarding the biological disorders of coagulation in these patients. The purpose of this project is to analyze hemostasis and coagulation of patients with infection of COVID-19 and severe pneumonia.	Primary outcome: -Variation of thrombin time in COVID-19 patients admitted to the ICU (time frame: up to 6 weeks) -Variation of factor V, factor II, fibrin, and fibrinogen in COVID-19 infected patients in ICU
26	Utilização da Enoxaparina em Dose Anticoagulante em Pacientes Hospitalizados Com síndrome respiratória Aguda Grave Por COVID-19/Juni *et al.*/NCT04444700	Recruiting	Interventional (clinical trial): intervention tested: therapeutic anticoagulation with enoxaparin	462	Published papers evaluating coagulopathy on COVID-19 patients indicate a higher incidence of thromboembolic events, sometimes, as high as 20%. Such events increase ICU admissions and are associated with death. This study aims to determine the effect of therapeutic anticoagulation compared to standard care in hospitalized patients with COVID-19 and with low oxygen saturation.	Primary outcome: -Composite main outcome (time frame: up to 28 days) -Composite outcome of ICU admission (yes/no), non-invasive positive pressure ventilation (yes/no), invasive mechanical ventilation (yes/no), or all-cause death (yes/no) up to 28 days.
27	Impact of Implementation of an Intensified Thromboprophylaxis Protocol in in Critically Ill ICU Patients With COVID-19: a Longitudinal Controlled Before-after Study/Jessa Hospital/NCT04394000	Completed	Observational (patient registry)	72	The main goal of this study is to investigate and compare the mortality, the incidence of DVT and the incidence of kidney and liver failure in patients admitted to ICU before and after intensified thromboprophylaxis protocol on 31st of March 2020.	Primary outcome: -2 week mortality (time frame: 2 weeks after admission at ICU) Secondary outcome: -The incidence of DVTs, kidney failure, and liver failure in COVID-19 patients admitted to the ICU before and after the implementation of the thromboprophylaxis protocol.
28	COVID-19 and Deep Venous Thrombosis: a Cross-sectional Study/Jessa Hospital/NCT04338932	Completed	Observational	12	This study aims to investigate the prevalence, and identify possible risk factors of, DVT's in patients intubated and mechanically ventilated at the ICU. Parameters include demographics, comorbidities, symptoms, lab results, treatment, complications, ventilation, and radiological findings.	Primary outcome: -The prevalence of a DVT in patients at the ICU (time frame: 1 day at ICU)
29	Patient Characteristics, Outcome and Thromboembolic Events Among Adult Critically Ill COVID-19 Patients With Different Anticoagulant Regimes at One of the Biggest Emergency Hospitals in Northern Europe, Sweden/Cronhjort *et al.*/NCT04412304	Completed	Observational	166	This study aims to compare anticoagulation regime with outcome in critically ill patients with COVID-19 by describing baseline characteristics and comorbidities, level of organ support, and dose of anticoagulation treatment.	Primary outcome: -28 days ICU mortality (time frame: 28 days from ICU-admission) Secondary outcome: -Incidence of thromboembolic events -Incidence of bleeding events -ICU free days alive from ICU admission
30	Incidence and Characteristics of Pulmonary Embolism in COVID-19 Patients Hospitalized for Acute Respiratory Syndrome/Groupe Hospitalier Paris Saint Joseph/NCT04420312	Completed	Observational	1,024	Strikingly high D-dimers levels have been early reported in COVID-19 patients and have been associated with increased mortality. A single observational study suggests that anticoagulation is associated with a decreased mortality in severe COVID-19 patients. This is a multicentric case-control study that aims at evaluating the prevalence of pulmonary embolism and associated clinical outcomes.	Primary outcome: -Impact of pulmonary embolism on COVID-19 patients (time frame: March 1st, 2020) Secondary outcome: -Clinical and radiological characteristics

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
31	Risk of Venous Thromboembolism in Critically Ill Patients With Severe COVID-19/Bellmunt *et al.*/NCT04374617	Completed	Observational	230	The aim of this study is to determine the cumulative incidence of VTE in critically ill patients with COVID-19 and its impact on prognosis by performing a cut-off screening of deep venous thrombosis (DVT) with bilateral duplex ultrasound in 230 patients.	Primary outcome: -Venous thromboembolisms (time frame: 7 days) Secondary outcome: -Deaths from all causes during the follow-up
32	A Multicenter, Randomized-Controlled Trial to Evaluate the Efficacy and Safety of Antithrombotic Therapy for Prevention of Arterial and Venous Thrombotic Complications in Critically-Ill COVID-19 Patients/Morrow *et al.*/NCT04409834	Not yet recruiting	Interventional (clinical trial): intervention tested: drugs (unfractionated heparin iv, enoxaparin, clopidogrel, unfractionated heparin sc, enoxaparin 40 mg/0.4 mL injectable solution)	750	This is a multicenter, open-label, 2x2 factorial, randomized-controlled trial of critically ill patients with COVID-19 that evaluates the efficacy and safety of full-dose vs standard prophylactic dose anticoagulation and of antiplatelet vs. no antiplatelet therapy for prevention of venous and arterial thrombotic events	Primary outcome: -Venous or arterial thrombotic events (time frame: 28 days or until hospital discharge, whichever earlier) -Hierarchical composite: Death due to venous or arterial thrombosis, pulmonary embolism, clinically evident DVT, type 1 MI, ischemic stroke, systemic embolism or acute limb ischemia, or clinically silent DVT Secondary outcome: -Clinically evident venous or arterial thrombotic events -Hierarchical composite: Death due to venous or arterial thrombosis, pulmonary embolism, clinically evident DVT, type 1 MI, ischemic stroke, systemic embolism or acute limb ischemia
33	A Randomized, Open-Label Trial of Therapeutic Anticoagulation in COVID-19 Patients With an Elevated D-Dimer/Albaghdadi *et al.*/NCT04377997	Not yet recruiting	Interventional (clinical trial): intervention tested: enoxaparin	300	The aim of this randomized, open-label trial is to look at therapeutic anticoagulation in COVID-19 patients with an elevated D-dimer and evaluate the efficacy and safety.	Primary outcomes: -Number of patients with the composite efficacy endpoint of death, cardiac arrest, symptomatic deep venous thrombosis, pulmonary embolism, arterial thromboembolism, myocardial infarction, or hemodynamic shock (time frame: 12 weeks) -Number of patients with a major bleeding event according to the International Society of Thrombosis and Hemostasis (ISTH) definition
34	Effect of Anticoagulation Therapy on Clinical Outcomes in Moderate to Severe Coronavirus Disease 2019 (COVID-19)/Landmesser *et al.*/NCT04416048	Not yet recruiting	Interventional (clinical trial): intervention tested: rivaroxaban vs standard of care	400	This is a multicenter, prospective, randomized, event-driven study that evaluates rivaroxaban compared with standard of prophylactic anticoagulants.	Primary outcome: -Composite endpoint of venous thromboembolism (DVT and/or fatal or non-fatal PE), arterial thromboembolism, new myocardial infarction, non-hemorrhagic stroke, all-cause mortality or progression to intubation and invasive ventilation (time frame: 35 days post randomization)
35	Enoxaparin for Primary Thromboprophylaxis in Ambulatory Patients With Coronavirus: The Multicenter Randomized Controlled Ovid Trial/Kucher *et al.*/NCT04400799	Not yet recruiting	Interventional (clinical trial): intervention tested: enoxaparin	1,000	The study is a multicenter randomized open-label controlled trial and its hypothesis is that early thromboprophylaxis may prevent or limit coagulopathy, and reduce thromboembolic complications leading to hospitalization or death, in the presence of mild COVID disease among outpatients.	Primary outcome: -Hospitalizations (time frame: 30 days) -All-cause death Secondary outcome: -Number of cardiovascular events, any hospitalizations, all-cause death, net clinical benefit, disseminated intravascular coagulation
36	Exploratory Assessment of the Coagulation Changes Associated With Severe Inflammation in COVID-19 Patients/HemoSonics LLC/NCT04460664	Not yet recruiting	Observational	50	This single center, prospective, observational pilot study aims to characterize changes in coagulation status of patients with COVID-19 infection during their hospital stay. The QPlus Cartridge can measure hypercoagulable and hypo-coagulable conditions resulting from the functional interaction of the enzymatic and cellular components of coagulation and therefore, can be invaluable for longitudinal monitoring of the coagulopathies reported in COVID-19 patients and the response to anticoagulants.	Primary outcome: -Quantra clot time results (time frame: within 24 hours of admission to the hospital) -Quantra stiffness results

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
37	Incidence of Deep Vein Thrombosis at Doppler Echo in Patients With SARS-Cov-2 Pneumopathy Hospitalized in ICU/Maruizot *et al.*/NCT04363528	Not yet recruiting	Interventional (clinical trial): intervention tested: doppler echo	50	The main objective of the study is to determine the incidence of deep vein thrombosis at Doppler echo in patients with SARS-Cov-2 pneumopathy upon their entry into ICU and after 7 days of hospitalization in ICU.	Primary outcome: -Incidence of DVTs (time frame: day 0 and 7 of ICU admission)
38	Increased Risk of Venous Thromboembolism and Higher Hypercoagulable State in Patients Recovered in Intensive Care Unit and in Medical Ward for Coronavirus Disease 2019 (COVID-19)/Simioni *et al.*/NCT04359212	Not yet recruiting	Observational	90	The aim of this study is to verify if patients admitted to hospital in a medical division and in the ICU for a COVID-19 infection are at a higher risk of developing VTE complication and if they actually present an increased hypercoagulable state.	Primary outcome: -Cumulative proportion of any distal or proximal deep venous thrombosis or of a symptomatic pulmonary embolism (time frame: 28 days) Secondary outcome: -Cumulative proportion of any distal or proximal deep venous thrombosis or of symptomatic pulmonary embolism plus the asymptomatic incidentally detected pulmonary embolism
39	Investigating the Relationship Between the Renin Angiotensin System and the Coagulopathy Associated With COVID-19/Owen *et al.*/NCT04419610	Not yet recruiting	Interventional (clinical trial): intervention tested: TRV027 peptide for infusion vs NaCl placebo comparator for infusion	60	The aim of this study is to determine whether the coagulopathy associated with COVID-19 infection is driven by overactivation of the renin angiotensin system (RAS). AngII and Ang(1-7) affect various aspects of the coagulation system including platelets and endothelial cells, and therefore, the hypothesis is that overactivation of RAS is partly responsible for the coagulopathy present in COVID-19 infection. TRV027 is a similar peptide to Ang(1-7) but is a much more potent biased agonist at AT1R than Ang(1-7) and would be expected to oppose the effects of AngII accumulation, and functionally correct the Ang(1-7) deficiency.	Primary outcome: -Coagulopathy associated with COVID-19 (time frame: day 1 and day 8)
40	Prasugrel in the Prevention of Severe SARS-CoV2 Pneumonia in Hospitalised Patients/Azienda Ospedaliera Universitaria Integrata Verona/NCT04445623	Not yet recruiting	Interventional (clinical trial): intervention tested: Prasugrel Hydrochloride 10 MG Oral Tablet vs placebo	128	The hypothesis of this study is that COVID-19 platelet activation occurs via an inflammation-dependent mechanism and that early antithrombotic prophylaxis in non-critical patients, like those admitted to medical wards, could reduce the incidence of pulmonary thrombosis as well as respiratory and multi-organ failure, contributing to improve clinical outcome of the patients with pneumonia caused by SARS-COV2 viruses.	Primary outcome: -P/F ratio at day 7 (time frame: day 7) Secondary outcome: -Daily P/F ratio (time frame: 15 days) -Venous thrombosis/pulmonary embolism/thrombosis
41	Randomised Controlled Trial Comparing High Versus Low LMWH Dosages in Hospitalized Patients With Severe COVID-19 Pneumonia and Coagulopathy Not Requiring Invasive Mechanical Ventilation/Marietta *et al.*/NCT04408235	Not yet recruiting	Interventional (clinical trial): intervention tested: enoxaparin	300	The goal of this study is to assess whether high doses of low molecular weight heparin compared to standard prophylactic dose are more effective to prevent clinical worsening and are similar in terms of major bleeding risk during hospital stay.	Primary outcome: -Clinical worsening (time frame: through study completion, up to 30 days) Secondary outcome: -Mortality at 30 days (time frame: 30 days)
42	Thrombosis Risk Assessment May Predict Clinical Presentation and Length of Hospital Stay in Covid-19 Pneumonia/Civan et al./NCT04423315	Not yet recruiting	Observational	70	The aim of this study is to investigate the association between thrombosis risk and clinical presentation of COVID-19. The investigators aimed to find out potential associations between markers of prothrombotic or inflammatory conditions and some clinical features of COVID-19 pneumonia cases on admission and follow-up.	Primary outcome: -Length of hospital stay (time frame: 2 months)

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Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
43	Crizanlizumab for Treating COVID-19 Vasculopathy/ Lowenstein *et al.*/NCT04435184	Not yet recruiting	Interventional (clinical trial): intervention tested: Crizanlizumab	40	The aim of this study is to test the efficacy and safety of crizanlizumab in decreasing biomarkers of inflammation and thrombosis in a placebo-controlled, double-blind randomized clinical trial.	Primary outcome: -Soluble P-selectin level (time frame: day 1 after randomization) Secondary outcome: -Soluble P-selectin levels, D-dimer levels, VWF levels, CRP levels, change in clinical status as assessed by the WHO Ordinal Scale for COVID-19 trials, time to hospital discharge, safety of crizanlizumab as assessed by adverse events
44	Investigation of Systemic Microvascular Flow and Reactivity in Patients Presenting in the Acute Phase of Coronavirus Disease-19./Tibirica *et al.*/NCT04406545	Recruiting	Observational	25	This study aims to investigate the presence of endothelial dysfunction in patients with COVID-19, also evaluating associations between the presence of endothelial dysfunction and demographic, clinical, and laboratory variables.	Primary outcome: -To evaluate, through laser doppler, the presence of changes in systemic microvascular endothelial function in patients in the acute phase of COVID-19 (time frame: Microvascular reactivity will be evaluated after a 20-minute rest in the supine position in a temperature-controlled room)
45	Thrombo Embolic Events in Hospitalized Patients With Covid-19 Serious Acute Pneumopathy/Slama *et al.*/ NCT04377490	Recruiting	Observational	100	The purpose of this project is to analyze hemostasis and coagulation of every hospitalized patient with infection of COVID-19.	Primary outcomes: -Variation of thrombin time (in seconds) in Hospitalized Covid-19 patients (time frame: up to 6 weeks) -Variation of factor V concentration -Variation of factor II concentration -Variation of concentration of fibrin and fibrinogen degradation
46	Evaluation of the Role of Sonoclot Coagulation and Platelet Function Analyzer in Assessment of Coagulopathy in Critically Ill COVID-19 Patients.	Recruiting	Observational	50	Coagulopathy is one of the most significant prognostic factors in patients with COVID-19 and is associated with increased mortality and admission to critical care. Most observed coagulopathy in patients hospitalized with COVID-19 is characterized by increased D-dimer and fibrinogen levels. They will use the sonoclot on COVID positive patients and a COVID negative control group to describe differences in the rate of clot formation.	Primary outcome: -Clot rate formation (time frame: 30 minutes)
47	Evaluation of the Role of Sonoclot Coagulation and Platelet Function Analyzer in Assessment of Coagulopathy in Critically Ill COVID-19 Patients./Abdelaal *et al.*/NCT04479280	Recruiting	Observational	12,000	The aim of this study is to investigate the prevalence of VTE in a regional healthcare system prior to, and during the SARS-CoV-pandemic and the differences between ICU, hospitalized and outpatient cohorts.	Primary outcome: -Is there an increased prevalence of venous thromboembolism in a regional healthcare system in Sweden during the SARS-CoV-2 pandemic? (time frame: March to May in 2020) -Is a SARS-CoV-2-infection an isolated risk factor for thromboembolism?
48	Assessment of Endothelial and Haemostatic Changes During Severe SARS-CoV-2 Infection/Ebesnier *et al.*/NCT04357847	Recruiting	Observational	100	The outbreak at covid-19 is caused by the SARS-CoV-2 virus. This virus can be responsible for severe respiratory failure but also for extra-respiratory organ dysfunctions associated with severe inflammatory stress.	Primary outcome: -Association of InterCellular Adhesion Molecule-1 plasma level with 28 days mortality (time frame: 24 hours)
49	Assessment of the Risk of Pulmonary Embolism and Coagulation Profile in Patients With SARS Coronavirus (COV-2) Lung Disease/Tcherakian *et al.*/NCT04479540	Recruiting	Interventional (clinical trial): intervention tested: angiography scanner	120	The main objective is to study the coagulation and fibrinolysis profile in these patients and to assess endothelial activation in order to better understand the phsyio-pathological mechanism behind PE and to determine if one of the parameters studied could be an indicator of PE risk.	Primary outcome: -Rate of PE in COVID-19 patients (time frame: Day 0-12) Secondary outcome: -Prothrombin level measurements -aPTT level measurements -Fibrinogen measurements

Table S1(*continued*)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
Arrythmia related studies						
50	Cardiac Arrhythmias In Patients With Coronavirus Disease (COVID-19)/Reddy *et al.*/NCT04358029	Recruiting	Observational	10,000	Improved characterization of arrhythmia burden and mechanism of death is critical, primarily in guiding the need for developing treatment strategies as some current treatment modalities have increase arrhythmogenic potential.	Primary outcome: -Frequency of cardiac arrhythmias (time frame: 19 months) Secondary outcome: -Mode of death
51	The ACOVID-19 Study - A Prospective Cohort Study Investigating the Acute Effect of COVID-19 on the Heart by Continuous ECG Monitoring/Lamberts *et al.*/NCT04395664	Recruiting	Observational	1,000	The investigators aim to examine if continuous ECG monitoring can be used to understand the contribution of COVID-19 infection in the acute phase to the development of cardiac arrhythmias, especially focusing on cardiovascular outcomes. In all patients included, the investigators aim to examine if continuous ECG monitoring - alone and in combination with biomarkers - can be used to detect early signs of cardiac complications and predict long-term risk of cardiovascular morbidity and mortality following COVID-19 infection.	Primary outcome: -In-hopsital mortality during hospitalization and a confirmed COVID-19 diagnosis (time frame: 4 months) -Incident ICU admission during hospitalization and a confirmed COVID-19 diagnosis
52	COVIDAR - International Registry on Arrhythmias in COVID-19/Arbelo *et al.*/NCT04437901	Not yet recruiting	Observational (patient registry)	10,000	This study aims to describe the incidence and type of arrhythmic events in the context of the SARS-CoV infection.	Primary outcome: -Arrhythmia (time Fame: from date of admission until the date of first documented arrhythmic adverse event or date of death from any cause, whichever came first, assessed up to 12 months) Secondary outcome: -Electrocardiographic changes (underlying rhythm, atrioventricular conduction, QRS duration, presence of Brugada QRS patter, QTc duration) -Lab abnormalities (electrolyte misbalance, cardiac biomarkers, renal function, liver function)
53	Remote Monitoring in Patients With Coronavirus Disease (COVID-19)/Reddy *et al.*/NCT04350476	Not yet recruiting	Interventional (clinical trial): intervention tested: VitalConnect Vital Sign Patch which is a home monitoring system	1,000	The aim of this study is to assess the impact of remote cardiac and vital sign monitoring in patients with COVID-19 in the outpatient setting.	Primary outcome: -Number of different arrhythmias (time frame: 7-14 days) -Temperature -Oxygen saturation
CVD comorbidity and effect on COVID-19 related studies						
54	Cardiac Complications in Patients With SARS Coronavirus 2 Registry/Asselbergs *et al.*/NCT04325412	Recruiting	Observational (patient registry)	1,000	The aim of CAPACITY is to collect data regarding the cardiovascular history, diagnostic information and occurrence of cardiovascular complications in COVID-19 patients in order to aid in providing more insight in (1) the incidence of cardiovascular complications in patients with COVID-19, and (2) the vulnerability and clinical course of COVID-19 in patients with an underlying cardiovascular disease.	Primary outcome: -The incidence of cardiovascular complications in patients with COVID-19 (time frame: 30 days)
55	Characterization of Cardiovascular Diseases and Risk Factors in Patients With Suspected SARS-CoV2/Covid-19 Infection/Rassaf *et al.*/NCT04327479	Recruiting	Observational (patient registry)	728	This study aims to characterize the effect of pre-existing cardiovascular conditions on mortality in patients with COVID-19 infection.	Primary outcome: -All cause mortality (time frame: during 1 year follow-up) Secondary outcome: -30- day mortality (time frame: within 30 days after inclusion) -Major adverse cardiovascular events (time frame: during 1 year follow-up)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
56	COVID-19 in Hospitalised Patients With Preexisting Cardiovascular Diseases and/or Cardiac Involvement and/or Cardiovascular Risk Factors: the Global PCHF-COVICAV Registry/Flammer *et al.*/NCT04390555	Recruiting	Observational (patient registry)	1,500	Patients with cardiovascular diseases, heart failure in particular, and cardiovascular risk factors seem to be at a very high risk if affected by COVID-19 - and vice versa there are more and more reports of cardiac manifestations with the viral disease. This study looks at the effect that comorbid cardiovascular conditions have on the COVID-19 disease course.	Primary outcome: -In-hospital mortality (time frame: Hospitalization period, assessed up to 30 days) -All-cause and cardiovascular mortality during index hospitalization.
57	Impact of Covid-19 in Congenital Heart Disease - COVID-CHD/Amedro *et al.*/NCT04336384	Recruiting	Observational	5,000	Cardiovascular disease appears to be a risk for severe COVID-19 infection. The population of congenital heart disease (CHD) might also be at risk, however, no data is available in this group of patients. This study aims to assess the morbidity, the mortality and the risk factors associated with Covid-19 in patients with CHD in France.	Primary outcome: -Prevalence of COVID-19 infection in the overall CHD population (time frame: through study completion, an average of 2 weeks)
58	Impact of COVID19 Outbreak in Cardiac Patients Admitted in Intensive Care Unit: the CCU-COVID19 Study/Silvain *et al.*/NCT04344912	Recruiting	Observational (patient registry)	500	This registry will evaluate the impact of the COVID19 outbreak on cardiac patients admitted in the ICU of the Pitie-Salpetriere Hospital in Paris, France.	Primary outcome: -Incidence of recurrent major cardiovascular events (MACE) and urgent rehospitalization (time frame: from admission to one year follow up)
59	Prospective Observational ICU Trial in Critical Ill COVID-19 Patients (POINT-C) Cardiovascular Risk and the Effects on Myocardial Events in Critical Ill COVID-19 Patients/Rief *et al.*/NCT04349982	Recruiting	Observational (patient registry)	50	The aim of this study is to observe the intensive care course in 30-50 COVID-19 patients with regard to cardiovascular risk factors and biomarkers.	Primary outcome: -ICU CV risk and Biomarker (e.g., Troponin) (time frame: through study completion, up to 4 weeks) Secondary outcome: -CV risk and Outcome during ICU stay
60	Qatar Cardiovascular COVID-19 Registry/Al Suwaidi *et al.*/NCT04430374	Recruiting	Observational (patient registry)	100	Described in the initial data, COVID-19 infection poses increased risk to patients with cardiovascular comorbid conditions. This study aims to assess patients with cardiac disease with COVID-19 in Qatar and the acute myocardial infarction with COVID-19 from the Gulf countries and collect all the related data to come with a comprehensive view about those patients.	Primary outcome: -The impact of COVID-19 on cardiovascular patient (time frame: 2 month from starting date)
61	Changes in Organ Specific Biomarkers, Virus Expression and Prognosis of Covid-19/University Hospital, Akershus/NCT04314232	Recruiting	Observational	200	Covid-19 is associated with a wide range of symptoms and clinical trajectories, and early identification of patients at risk for developing severe disease is desirable. This study aims to assess the prognostic value organ specific biomarkers, viral dynamics and immune response markers in patients infected with SARS-CoV2.	Primary outcome: -Number of participants with ICU admission or death (time frame: From hospital admission (baseline) until the date of either admission to the ICU or death during the index hospitalization (up to 52 weeks))
62	Risk Factors, Personalized Prognoses and 1-year Follow-ups of Patients Admitted to Spanish Intensive Care Units Due to COVID-19/Torres *et al.*/NCT04457505	Recruiting	Observational (patient registry)	5,000	This study aims to characterize the risk factors associated with patients who develop severe disease and have high mortality rates. Amongst other things the investigators explore how cardiac comorbid conditions affect outcomes in COVID-19.	Primary outcome: -One year mortality (time frame: At 12 months of ICU admission) -Six month mortality (time frame: At 6 month of ICU admission)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
63	Early Risk Stratification of Patient Hospitalized for SARS-CoV2 Infection: Critical COVID-19 France CCF/Bonnet *et al.*/NCT04344327	Completed	Observational	2,878	This study aims to identify early predictors of clinical worsening in patients hospitalized for COVID-19 in the cardiology or conventional medicine department. Clinical data relating to history, comorbidities, risk factors, treatments, clinical parameters, biological and cardiological data, procedures and events during hospitalization will be recorded.	Primary outcome: -Death rate (time frame: through study completion, an average of 4 weeks) -transfer to ICU -ventilation analysis Secondary outcome: -Construction of a predictive score for COVID-19 severe form
64	Accurate Classification System for Patients With COVID-19 Based on Prognostic Nomogram/Gong *et al.*/NCT04302688	Completed	Observational	669	In this study, a COVID-19 pneumonia grading scale was set up and the score system was validated to predict the clinical outcome of a patient. This grading system was compared with SEPSIS and CURB-65 grading system. The investigators specifically aim to describe the effect of cardiac comorbid conditions on COVID-19 mortality.	Primary outcome: -Survival status (time frame: 10 December 2019 to 10 February 2020)
65	Time of Recovery and Prognostic Factors of COVID-19 Pneumonia/Mingrone *et al.*/NCT04324684	Completed	Observational	198	This study will assess the recovery rate in patients with COVID-19 pneumonia with certain comorbidities. Comorbidities include hypertension, obesity and/or type 2 diabetes, cardiovascular disease, and chronic obstructive lung disease.	Primary outcome: -Rate of recovery (time frame: 3 weeks) Secondary outcome: -Time to improvement -Efficacy of treatments -Organ failure
66	Cardiovascular Disease, Cardiovascular Risk Factors, Treatments and Severe COVID-19 Outcomes. A Nationwide Registry-based Case-Control Study/Karolinska Institutet/NCT04426084	Active, not recruiting	Observational (patient registry)	22,784	This study cross-references several nationwide high-quality Swedish registers in order to study risk factors and the effect they have on outcomes for severe COVID-19, with a focus on cardiovascular disease, different treatments and socioeconomic factors.	Primary outcome: -Severe Covid-19 (time frame: 2020-03-01 to 2020-05-11) -Severe COVID-19 with pulmonary embolism Secondary Outcome: -CRRT(Continuous Renal Replacement Therapy) -ECMO (Extracorporeal Membrane Oxygenation) -ICU Mortality
67	Coronavirus Disease 19 Survival - The COVIVA Study/Twerenbold *et al.*/NCT04366765	Recruiting	Observational	1,500	This study aims to i) perform extensive clinical and biomarker phenotyping in COVID-19 suspects presenting to the emergency department (ED) as well as admitted to the intensive care unit, ii) compare clinical and biomarker profiles of COVID-19 patients with a control group, iii) derive and validate personalized risk prediction models for early clinical decision support, and iv) explore pathophysiological mechanisms.	Primary outcome: -Short-term prognosis (time frame: at 30 days)
68	Cardiovascular Risk in COVID-19 Patients: Metabolic, Prothrombotic and Proinflammatory Mechanisms Associated With Outcome and With Cardiorespiratory Features During the Acute Viral Disease and at Short Term Follow-up/Parati *et al.*/NCT04371289	Not yet recruiting	Observational	5,500	The goals of this study are to comprehensively assess risk factors for severe COVID-19 syndrome, study pathophysiology of its cardio-respiratory manifestations, estimate risk scores using artificial intelligence, and assess its clinical immunoinflammatory and cardiorespiratory sequelae in discharged patients at short term follow-up.	Primary outcome: -predictive modeling of in-hospital outcome (time frame: 12 months) -clinical, pathophysiological and molecular mechanisms -short-term sequelae

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
69	Impact of Comorbidities on COVID19 Outcome/Hassan *et al.*/NCT04459390	Not yet recruiting	Observational	100	The aim of this study is to assess the impact of comorbidities in patients with diagnosis of COVID-19 on outcome, in order to find the predicator of prolonged hospital stay, need for ICU admission or poor outcome.	Primary outcome: -rate of recovery/ICU admission/need for mechanical ventilation (time frame: baseline) -time to improvement
70	WHF COVID-19 and Cardiovascular Disease Survey/Silwa *et al.*/NCT04475471	Recruiting	Observational	5,200	The aim of this global study is to better understand cardiovascular conditions that increase the risk of developing severe COVID-19, and a better characterization of cardiovascular complications in hospitalized patients with COVID-19.	Primary outcome: -Assessment of the patients for major adverse cardiovascular events (MACE) (time frame: Outcome will be assessed at discharge and 30-day follow-up visit) -Assessment of the patients for Pulmonary outcomes including Pulmonary embolism, pneumonia, acute respiratory distress syndrome, need of intensive care - number of days in ICU or ICCU, need of ventilator -Assessment of the patients for Neurological Outcomes including stroke and Transient Ischemic Attack (TIA) -All cause deaths
Myocarditis related studies						
71	Cardiovascular and Pulmonary Imaging in SARS-CoV-2: A Study of the Heart, Lungs and Wellbeing After COVID-19./Berry *et al.*/NCT04403607	Recruiting	Observational	180	COVID-19 places patients at high risk for myocardial injury. This study uses cardiac imagin (MRI and CTA coronary) at 28 days post discharge to identify the number of patients with myocardial inflammation (myocarditis).	Primary outcome: -Proportion of patients with a diagnosis of myocardial inflammation (myocarditis) (time frame: 28 days after discharge from hospital)
72	Hospital Registry of Acute Myocarditis: Evolution of the Proportion of Positive SARS-COV-2 Cases During the Covid-19 Pandemic, Case Characteristics and Prognoses/Delmas *et al.*/NCT04375748	Recruiting	Observational	400	A significant association was found between troponin elevation, and that of CRP and NtproBNP, suggesting an inflammatory part to this cardiac damage. In the context of the viral pandemic at Covid19, although few data exist, it is legitimate to consider the possibility of true arrays of acute inflammatory myocarditis or by direct viral attack which could thus modify the natural history and the prognosis of patients.	Primary outcome: -Assess the proportion of positive SARS-CoV-2 cases among the patients included (hospitalized for acute myocarditis) (time frame: 1 year)
73	Imaging Cardiac Phenotype of SARS-Cov-2 (Covid19) Infected Patients/Minville *et al.*/NCT04358952	Recruiting	Observational	50	The objective of this study is to define cardiac phenotype in covid using comprehensive cardiac imaging tools of patients infected with Covid 19 in order to explore the functional impact of the infection on the myocardium. Patients with biological myocardial involvement will be followed to determine the evolution of their myocardial functional parameters during the course of the infection.	Primary outcome: -left ventricular function (time frame: Day 0,3,7) Secondary outcome: -inflammatory biological parameters
74	Cardiac Involvement in Coronavirus (SARS-Cov-2) Infected Health Care Workers: The CCC Study/Sanchez *et al.*/NCT04413071	Completed	Observational	142	The aim of this study is to look at prevalence of myocardial damage suggestive of myocarditis and the prevalence of pericarditis in HUSA healthcare workers during a 3 month period. These will be related to the systemic immune response to SARS-CoV-2.	Primary outcome: -Myocarditis and pericarditis incidence (time frame: up to 3 months) Secondary outcome: -Atrial fibrillation -Ischemic heart disease -Dilatation of right hear chambers -Valvular heart disease -Rhythm disorders

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Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
75	Uncovering the Cardiac Phenotype of Individuals With SARS-COV-2 and Cardiac Injury/Grodin *et al.*/NCT04435457	Not yet recruiting	Observational (patient registry)	70	The aim of this study is to better understand the epidemiology of cardiac injury in acutely ill COVID-19 patients through deep cardiac phenotyping and identify the molecular profile of individuals most susceptible to cardiac injury from COVID-19.	Primary outcomes: -prevalence of myocarditis (time frame: up to 4 weeks) Secondary outcomes: -prevalence of cardiac abnormalities by cardiac magnetic resonance imaging -prevalence of molecular and genetic immune system abnormalities
Cardiac injury related studies						
76	Acute Cardiovascular Events Triggered by COVID-19-Related, Non-infectious Stress The Jordan COVID-9 caRdiovascular Events (JoCORE) Study/Hammoudeh *et al.*/NCT04368637	Recruiting	Observational	50	Acute coronary events are often triggered by emotional/stressful events. This observational study aims to assess the incidence of acute cardiovascular events triggered by COVID related stress.	Primary outcome: -Acute cardiovascular event triggered by COVID-19 stress (time frame: 4 months) -Ventricular tachycardia -Acute stroke -Implantable cardioverter defibrillator
77	An Observational Study of Hospitalised Patients With Coronavirus Disease 2019 (COVID-19) to Determine the Degree of Myocardial Injury Using Biomarkers and Echocardiography, and the Impact of This on Cardiovascular Outcomes/Weir *et al.*/NCT04438993	Recruiting	Observational	100	The primary objective of the study is to evaluate the prevalence of myocardial injury and cardiac dysfunction in patients admitted to the hospital with COVID infection. Several biomarkers will be collected (Troponin, pro-BNP and ferritin) as well as an ECG and echocardiogram.	Primary outcome: -Cardiac abnormalities in COVID-19 positive inpatients (time frame: 6 months) Secondary outcome: -Biomarker abnormalities in patients who experience adverse events compared to those who do not (time frame: 30 days)
78	Association of Early Myocardial Injury With Major Adverse Outcomes in Patients With COVID-19/Kini *et al.*/NCT04397939	Recruiting	Observational	5,000	The aim of the proposed study is to analyze the incidence, clinical outcomes, and predictors of myocardial injury in a large patient population with COVID-19 treated in Mount Sinai Hospital (MSH) system.	Primary outcome: -in-hospital death (time frame: During hospitalization, average 2-3 weeks) Secondary outcome: -length of stay
79	Cardiac Arrest Incidence and Outcome Among Patient With COVID-19 Pneumonia in French ICUs/Chelly *et al.*/NCT04373759	Recruiting	Observational (patient registry)	100	This study aims to report the incidence of ICUCA among patients hospitalized in French ICU for COVID-19 and to report the morbidity and mortality among COVID-19 patients admitted alive in ICU for an OHCA or an IHCA.	Primary outcome: -Incidence of unexpected cardiac arrest (time frame: 7 months)
80	Cardiovascular Manifestations of Hospitalized Patients With Coronavirus Disease 2019/Koutroumpakis *et al.*/NCT04335630	Recruiting	Observational	500	This study aims to describe the effects of COVID on the cardiovascular system. Cardiovascular disease associated with COVID-19 might be contributing to the high mortality rates and its recognition will allow for prevention, early diagnosis, and appropriate treatment. Laboratory evidence of myocardial injury, electrocardiographic changes, arrhythmias and echocardiographic abnormalities will be used to evaluate this.	Primary outcome: -Prevalence of cardiomyopathy, myocardial infarction, heart failure, clinically significant arrhythmias, cardiogenic shock or cardiac arrest (time frame: 1ne year)
81	Effect of Covid-19 Epidemic on Primary PCI and Prognosis in Patients With Acute STEMI/Li *et al.*/NCT04427735	Recruiting	Observational	200	During the pandemic there have been concerns that patients with STEMI requiring PCI may have poorer outcomes due to delays as a result of COVID testing. This study compares patients with STEMI requiring PCI to a group of patients during the same time in 2019 to assess outcomes.	Primary outcome: -MACE (major adverse cardiovascular events) (time frame: 1 year) -cardiovascular death, re-infarction, malignant arrhythmia, heart failure, revascularization, and stroke -all cause death

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
82	Identification of Predictors for the Evolution of COVID-19 Related Interstitial Pneumonia by Transcriptomic and Seroproteomic Techniques/Ranucci *et al.*/NCT04441502	Recruiting	Observational	240	This study aims to verify whether there are transcripts or cytokines / chemokines in peripheral blood, modulated differently in patients with COVID-19, distinguished on the basis of the evolution towards more severe clinical pictures that require patient intubation or that show signs of cardiovascular damage.	Primary outcome: -circulating markers for COVID-19 signature (time frame: from ICU/ward admission for 8 weeks follow up) Secondary outcome: -COVID-19 signature and adverse cardiovascular events COVID-19 related coagulation pattern
83	Impact of a Novel Coronavirus (2019-nCoV) Outbreak on Public Anxiety and Cardiovascular Disease Risk in China/Hao *et al.*/NCT04255940	Recruiting	Observational	12000	This survey aims to assess whether the public anxiety from a novel coronavirus (2019-nCoV) outbreak increases cardiovascular disease risk in China. Cardiovascular events occurring after 2019-nCoV outbreak in Jinan were prospectively assessed by emergency physicians and compared those events with events that occurred during the past 3 months and the same months of the last year.	Primary outcome: -cardiovascular death (time frame: 3 months) Secondary outcome: -major adverse cardiovascular events -times from symptom onset to hospital arrival -anxiety
84	Joint Use of Electrocardiogram and Transthoracic Echocardiography With Other Clinico-biological Parameters in an Observational Study to Monitor Cardio-vascular Events and Predict Outcomes in Patients Diagnosed With COVID-19/Salem *et al.*/NCT04320017	Recruiting	Observational	500	Cardiovascular events have possibly been highly underestimated. The study proposes to systematically collect cardio-vascular data to study the incidence of myocarditis and coronaropathy events during COVID-19 infection. The investigators also assess predictive factors for transfer in Intensive Care Unit or death.	Primary outcome: -Incidence of acute myocardial events in COVID-19 population at baseline and during hospital stay (time frame: ECG and concomitant troponin at day 1 after admission at day 1, day 3 day 6 the first week after admission, and then at day 14 and before the patient is discharged (up to 20 days))
85	Pathology and Pathogenesis of Cardiac Injury in COVID-19 Infections in Humans/Papa *et al.*/NCT04367792	Recruiting	Observational	50	The primary goal of the study is to conduct the first systematic cardiac autopsy study in >= 50 patients dying from COVID-19 to understand the pathology and pathogenesis of cardiac injury in patients with COVID-19, with/without cardiovascular comorbidities. Such data is essential for understanding rate of involvement, type of involvement and degree of injury in patients contracting the disease.	Primary outcome: -Cardiac pathological findings from series of >= 50 patients dying from COVID-19 disease (time frame: 1 year) -viral load in cardiac tissues and the extent of damage -Co-localize the SARS-CoV-2 using RNAscope in situ hybridization, with its entry receptor ACE2 and serine protease TMPRSS2 in different cell types found in the heart
86	Preventing Cardiac Complication of COVID-19 Disease With Early Acute Coronary Syndrome Therapy: A Randomised Controlled Trial./Kanagaratnam *et al.*/NCT04333407	Recruiting	Interventional (clinical trial): intervention tested: drugs (aspirin, clopidogrel, rivaroxaban, atorvastatin, omeprazole)	3,170	The severity of COVID-19 disease (as well as the likelihood of progression to severe disease) appears to be in part driven by direct injury to the cardiov ascular system. Randomizing patients to cardioprotective medicine will help us understand the role of the cardiovascular system in COVID-19 disease. It will also guide future treatment.	Primary outcome: -all cause mortality at 30 days after admission (time frame: at 30 days after admission)
87	Prediction of Acute Heart or Kidney Injury With Cardiovascular-renal Biomarkers in Patients Hospitalised for Severe or Critical Covid-19 Infection/Central Hospital, Nancy, France/NCT04354610	Recruiting	Interventional (clinical trial): intervention tested: -biological samples specific to research, -clinical examination, -telephone follow-up three months after discharge from hospital	57	The main objective of the Nancy Cov-H-AKI study is to evaluate the association of variations (from inclusion to 72H post-inclusion) of 5 blood-based cardio-vascular-renal biomarkers selected a priori, cardiac (NT-proBNP), coagulation (D-dimers), related to the renin angiotensin aldosterone system (ACE2) and renal (Penkid, and NGAL) with the appearance of acute kidney injury KDIGO grade 1 or higher OR cardiac injury in patients hospitalised for either the severe or the critical form of Covid-19.	Primary outcome: -Worsening of renal function by at least KDIGO grade 1 during hospitalization for Covid-19 infection (time frame: From inclusion to hospital discharge, an average of 21 days) -Troponin greater than 99th percentile during hospitalization for Covid-19 infection

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
88	Randomized, Open-Label, Controlled Trial of Colchicine to Reduce Cardiac Injury in Hospitalized COVID-19 Patients (COLHEART-19)/Ardehali *et al.*/NCT04355143	Recruiting	Interventional (clinical trial): intervention tested: colchicine tablets, other "current care" per UCLA treating physicians	150	This study investigates the potential cardio-protective effect of colchicine when added to standard of care. Participants will be randomized in a 1:1 ratio to receive Colchicine plus current care per UCLA treating physicians versus current care per UCLA treating physicians alone (control arm). Importantly, this adaptive trial design allows for patients in either study arm to receive other investigational drugs for COVID-19 as new science emerges.	Primary outcome: -Composite of all-cause mortality, need for mechanical ventilation, or need for mechanical circulatory support (MCS) (time frame: 90 Days) Secondary outcome: -Delta (peak minus baseline) troponin level -Delta (baseline to peak) brain natriuretic peptide (BNP) level -Change in left ventricular ejection fraction (LVEF) on echocardiography -Delta (peak minus baseline) C-Reactive protein (CRP)
89	The ECHOVID-19 Study - A Prospective Cohort Study Investigating the Acute Effect of COVID-19 on the Heart and Lung by Ultrasound/Biering-Sørensen *et al.*/NCT04377035	Recruiting	Observational	1,000	The investigators aim to examine if echocardiography - both conventional and advanced - can be used to predict which patients will develop acute respiratory distress syndrome (ARDS) or other short-term acute complications, especially focusing on cardiovascular outcomes. In addition, using a novel technique of lung ultrasound (LUS), the investigators aim to analyze specific LUS-findings, and associate them with short-term prognosis and development of ARDS and long-term cardiovascular morbidity and mortality.	Primary outcome: -In-hospital mortality during hospitalization and a confirmed COVID-19 diagnosis (time frame: 2.5 months) -Incident ARDS (Adult Respiratory Distress Syndrome) and intensive care unit admission Secondary outcome: -incidence of myocardial infarct, cardiac arrest, heart failure, pulmonary embolism or stroke
90	The Prevalence of Pulmonary Hypertension, With or Without Right Ventricular Loading, in Patients With COVID-19 Who Are Being Treated With a Respirator in the Intensive Care Unit/Lönnqvist et al/NCT04459364	Recruiting	Observational (patient registry)	80	This study looks at the incidence of pulmonary hypertension in the setting of COVID-19 pneumonia with and without right ventricular loading. The researchers plan to use on site echocardiography to evaluate these patients.	Primary outcome: -Prevalence of pulmonary hypertension and right ventricular load in patients with COVID-19 treated in intensive care unit evaluated by routine echocardiography (time frame: Day 01)
91	The Role of Adaptive Immunity in COVID-19 Associated Myocardial Injury/Mohiddin *et al.*/NCT04340921	Recruiting	Observational	140	The laboratory plans to perform immunophenotyping of peripheral T-cells in patients with COVID-19 and complications (ARDS or myocardial injury) and map this against clinical patient outcomes. The aim is to determine if there is a specific T-cell immunophenotype associated with COVID-19 and/or complications, which can be used to inform prognosis and guide potential therapies.	Primary outcomes: -T-cell immunophenotype (time frame: 12 months from enrollment) Secondary outcomes: - Myocardial injury and mortality.
92	Cardiac Structural and Functional Characteristics in COVID-19: A Dynamic Echocardiographic Study/Pu *et al.*/NCT04352842	Completed	Observational	51	This study aims to use a dynamic echocardiography study to investigate cardiac structural and functional changes in patients with COVID-19 who were admitted to the ICU. They will also compare the cardiac characteristics between deceased and survived patients.	Primary outcome: death of any cause (time frame: From admission to April 8 2020 (cutoff day))
93	Retrospective Study of Myocardial Damage in COVID-19/Cheng *et al.*/NCT04312464	Enrolling by invitation	Observational	500	This study's goal is to investigate the clinical characteristics, incidence of myocardial injury, and effect of myocardial injury on the prognosis in COVID-19 patients.	Primary outcome: -The myocardial injury incidence (time frame: 75 days) Secondary outcome: -Clinical characteristics, Clinical course, Cardiovascular comorbidity, Analysis of causes of death

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
94	Influence of COVID-19 on Vascular Endothelial Function/ Radboud University/NCT04468412	Not yet recruiting	Observational	200	The aim of this prospective observational study is to investigate the predictive value of endothelial dysfunction, measured by carotid artery reactivity testing, for 1 year cardiovascular events in patients with past COVID-19 infection.	Primary outcomes: -endothelial dysfunction (time frame: CAR will be measured between 6 and 20 weeks and 1 year after recovery from COVID-19) Secondary outcomes: -major adverse cardiovascular events (MACE) (time frame: 1 year)
95	Multi-modality Imaging & Immunophenotyping of COVID-19 Related Myocardial Injury/Tarkin *et al.*/NCT04412369	Not yet recruiting	Observational	20	The aim of this study is to identify disease-specific patterns of myocardial injury in COVID-19 using non-invasive multi-modality cardiac imaging, paired with cytokine/chemokine testing, immunophenotyping of peripheral blood cells and coagulation profiles.	Primary outcomes: -number of participants with a diagnosis of COVID-19 related myocarditis, Type 1 or 2 myocardial infarction and/or other mechanism of cardiac injury confirmed by multi-modality imaging (time frame: baseline) Secondary outcomes: -comparison of a panel of inflammatory cytokines and immune cell profiles in patients categorized by cardiac diagnosis after imaging -comparison of a panel of blood coagulation markers in patients categorized by cardiac diagnosis after imaging
96	Myocardial Infarction Rates Overview During COVID-19 Pandemic In France: MODIF Study/Bonnet *et al.*/ NCT04357314	Not yet recruiting	Observational	80	The aim of this study is to investigate the rates and characteristics of patients presenting with acute myocardial infarction between March 1, 2020 to May 31, 2020 and compared those data with those of this year (2019).	Primary outcomes: -rates of patients presenting with acute myocardial infarction (time frame: 3 months [between March 1 to May 31, 2019 and between March 1 to May 31, 2020)] Secondary outcomes: -patient profile during admission for acute myocardial infarction -medical care times analysis -proportion of patients who underwent systemic thrombolysis
Long term sequela related studies						
97	A Single-center Registry and Embedded Interventional Study of the Effects of COVID-19 With and Without Treatment With AT-001 on Cardiac Structure and Function in Patients Hospitalized for Management of COVID-19 Infection/Katz *et al.*/NCT04365699	Recruiting	Interventional (Clinical Study): intervention tested: Aldose Reductase Inhibitor	500	The aim of this trial is to determine the effects of standard of care treatment vs. standard of care plus AT-001 on cardiac structure and function and in-hospital survival in patients hospitalized for management of COVID-19 infection.	Primary outcome: -Proportion of subjects with decreased left ventricular ejection fraction ≥10% from baseline at time of hospitalization (time frame: 30 days) -Assess the incidence of adverse events from the intervention. Secondary objectives: -Change in left ventricular ejection fraction -Change in left ventricular end diastolic diameter -Biomarkers of cardiac injury -Incidence of atrial fibrillation -Frequency of ventricular arrhythmias
98	Long-term Effects of Coronavirus 2019 Disease on the Cardiovascular System in Patients Who Have Undergone a Diagnostic Nasopharyngeal Swab for SARS-CoV-2. CV COVID-19 Registry/Ortega Paz *et al.*/NCT04359927	Recruiting	Observational (patient registry)	10,000	Long-term cardiovascular outcomes of these patients are entirely unknown. The investigators aim to perform a registry of patients who have undergone a diagnostic nasopharyngeal swab for SARS-CoV-2 and determine their long-term cardiovascular outcomes.	Primary outcome: -cardiovascular mortality (time frame: 1 year) Secondary outcome: -acute myocardial infarction -stroke
99	The CardioPostCovid Study: Cardiovascular Consequences After COVID-19/Assistance Publique Hopitaux De Marseille"/ NCT04452630	Recruiting	Observational	200	The occurrence of cardiovascular complications in SARS-CoV-2 infections appears to be more frequent than in other viral respiratory infections. This study focused on the evaluation and the systematic cardiovascular follow up of patients who survived an episode of Covid-19, regardless of their cardiovascular profiles.	Primary outcome: -Presence of at least one clinical, biological and/or imaging cardiovascular anomaly within 1 month of recovering (time frame: 1 month)

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
100	Long-term Sequelae of Severe Sars-CoV-2 Infections University of Geissen NCT04442789	Recruiting	Observational	30	The long-term consequences of the strong inflammatory response affecting various organs are currently unknown. The effects on various organ systems are assessed post recovery. Cardiovascular assessment will include echocardiogram and electrogram.	Primary outcome: -Sequelae after COVID-19 (time frame: 12 months, extension if required)
101	The Assessment of the Prevalence, Clinical Course and Treatment of COVID-19 Complications/Gasior *et al.*/ NCT04453748	Enrolling by invitation	Observational	200	This study aims to assess the prevalence of particular complications after COVID-19 (ie pulmonary, cardiovascular, neurological, hepatic, and psychiatric disorders) and identify demographic and clinical risk factors of COVID-19 complications.	Primary outcome: -Prevalence of COVID-19 complications (time frame: 2 months) Secondary outcome: -Assessment of risk factors of COVID-19 complications (time frame: 2 months)
102	Opportunistic Screening for Asymptomatic Left Ventricular Dysfunction in COVID-19 Survivors/The University of Hong Kong/NCT04355884	Not yet recruiting	Observational	100	The aim of this prospective study is to evaluate the possible latent effects from COVID-19 in COVID-19 survivors.	Primary outcome: -new-onset cardiac arrhythmia (time frame: at the time of screening) -elevation of NT-proBNP -left ventricular dysfunction
103	Re-assessment After Hospitalization for Sars-COV-2 Infection: Standardized Assessment of Sequelae and Comorbidities 3 to 6 Months After Hospitalization/University Hospital, Montpellier/NCT04443257	Not yet recruiting	Observational	200	The aim of this study is to explore the sequelae of patients who have been hospitalized for acute SARS-CoV-2 infection, between 3 to 6 months after discharge from hospital, by characterizing the incidence of chronic respiratory failure and fibrosis, as well as of various comorbidities such as cardiovascular, metabolic, and psychological diseases.	Primary outcome: -development or worsening of a ventilatory disorder and/or chronic respiratory failure assessed by spriometry (time frame: 3 to 6 months after SARS CoV-2 infection) Secondary outcome: -Incidence of worsening of cardiovascular diseases, renal disease, liver disease, psychological pathology (anxiety, depression, post-traumatic stress, and insomnia) -Assessment of health related quality of life, fatigue, socioeconomic deprivation, development or worsening of metabolic disorders, auto-immune disorders
104	Registry of the Evolution of Diagnosed and/or Hospitalized Patients for Pulmonary Embolism During the Covid-19 Pandemic: Retrospective and Prospective Multicentric Study./Hospital St. Joseph, Marseille, France/NCT04465656	Not yet recruiting	Observational	250	The aim of this study is to classify all the complications occurring after the diagnosis of pulmonary embolism in patients tested initially COVID-19 positive and negative RT-PCR during the peak of the pandemic in France. The patients will be followed for 1 year in order to provide clinical and paraclinical data not yet published in the literature.	Primary outcome: -% of patients for each group presenting the occurrence of PE complications defined by the occurrence of at least ONE of the following events up to 6 months after PE diagnosis PE complications (time frame: 6 months after PE diagnosis) -chronic interstitial pathology -recurrence of PE -pulmonary hypertension -death
105	Become of Patients Infected or Suspected of Being Infected by Covid-19 and Supported by the GHPSJ and the Establishments of the Paris Plaisance Hospital City/Pilmis *et al.*/NCT04365530	Recruiting	Observational	2,000	The aim of this study is to study the long term sequela of patients infected with COVID-19 to guide future management of patients with this infection.	Primary outcome: -Clinical consequences of a Covid-19 infection in the care population (time frame: Year 2) Secondary outcome: -Risk factors at M6 (time frame: Month 6) -Risk factors at year 1 (time frame: Year 1) -Risk factors at year 2 (time frame: Year 2)
106	Analysis of Chronic Non-infectious Diseases Dynamics After COVID-19 Infection in Adult Patients/Arutyunov *et al.*/ NCT04492384	Recruiting	Observational	3,500	This study aims to analyze non-infectious diseases dynamics after SARS-CoV-2 infection in adults. It includes a retrospective analysis of medical histories and outcomes in adults with pre-existing conditions after SARS-CoV-2 infection and prospective monitoring of health status during 3, 6 and 12 months after discharge.	Primary outcome: -Rate of non-infectious diseases (time frame: 12 month since a moment of request of medical help) -Severity of COVID-19 depending on pre-existing diseases -Disability registration / change of disability status -Mortality

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Table S1(*continued*)

Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
107	Follow-up of Critical COVID-19 Patients (FUP-COVID)/Uppsala University/NCT04474249	Recruiting	Observational	300	The study will follow COVID-19 patients who required intensive care. The patients will be contacted after three to six months for a first follow-up with assessment of functional level in activities of daily life, psychiatric symptoms, neurological symptoms and working capacity as well as specific organ functions. The organ functions will include circulation, respiration, coagulation, immune function and kidney function. In addition, blood and urine will be collected for biobanking.	Primary outcome: -Mortality (time frame: within 90 days after admission to ICU) -Mortality (time frame: within 1 year after admission to ICU)
108	Hemodynamic Characteristics of Patients With SARS-CoV-2: PiCCOVID Study/Monnet *et al.*/NCT04337983	Recruiting	Observational	200	This study is a systematic assessment of cardiovascular system in COVID survivors, including echocardiography evaluating the left ventricular function and transpulmonary thermodilution of patients who survived COVID.	Primary outcome: -blood pressure (time frame: through study completion, an estimation of 6 months) -pulse (heart rate) Secondary outcome: -Incidence of new-onset or reversible systolic left ventricular dysfunction
Effect of COVID-19 on elective cardiac procedure related studies						
109	Randomized Controlled Trial of Digital Cardiac Counseling in Patients With Delayed Cardiac Surgical Treatment Due to Covid-19 Pandemic (DCC Trial)/Nia *et al.*/NCT04393636	Recruiting	Interventional (clinical trial): intervention tested: digital cardiac counseling	394	There are some studies showing an increased mortality associated with an increased waiting time for the patients on the waiting list for an elective cardiac surgery. The rationale for this study is to evaluate whether Digital Cardiac Counseling (DCC) would improve outcomes of the patients waiting for an elective cardiac operation. At the DCC platform, there will be assessments of cardiovascular symptoms, Covid-19 prevention for cardiovascular patients, smoking cessation, anxiety relief, exercise stimulation, pulmonary rehabilitation and diet adjustments.	Primary outcome: -MACEs (time frame: Cumulative incidence (from inclusion) at 1 year postoperatively) Secondary outcome: -all-cause mortality, cardiovascular related mortality, COVID-19 related mortality
110	Morbidity and Mortality Due to Deferral of Aortic Valve Replacement in Patients With Severe Aortic Stenosis - a Collateral Effect of the SARS-CoV-2 Pandemic (AS DEFER)/ Pilgram *et al.*/NCT04333875	Active, not recruiting	Observational (patient registry)	71	The COVID-19 pandemic has resulted in elective cardiac procedures being cancelled. The aim of this study is to investigate the effect of deferral of valvular replacement in patients with severe but not critical aortic stenosis on morbidity and mortality. The study will describe the rates of morbidity and mortality among patients with severe but not critical aortic stenosis in the interval from referral /indication for valvular replacement to intervention.	Primary outcome: Composite of all-cause mortality, disabling and non-disabling stroke, and hospitalization for heart failure (time frame: Assessed at 6 months after indication/referral for aortic valve replacement)
Effect of social isolation related studies						
111	Psychological Impact of Quarantine During the COVID-19 Outbreak and Worsening of Cardiovascular Risk in the French General Population: a Prospective Cohort Study/Berard *et al.*/NCT04397835	Recruiting	Observational	800	This study aims to assess risk factors for severe stress, anxiety or depression, during and after quarantine, as well as risk factors (including stress, anxiety or depression), in the worsening of cardiovascular risk. A telephone interview will be carried out during quarantine (V1), in the month following the end of quarantine (V2) and then, at 6 (V3) and 12 (V4) months.	Primary outcome: -worsening of cardiovascular risk (treatments, smoking consumption, food balance, weight gain, physical activity) (time frame: at 1, 6 and 12 month) Secondary outcome: -psychological impact of the quarantine on anxiety, stress, and health

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Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
112	COVID-19 Related Lockdown Effects On Chronic Diseases/ Centre Hospitalier Universitaire Dijon/NCT04390126	Active, not recruiting	Observational	1,200	The aim of this study is to assess the health impact of the containment related to the COVID-19 pandemic in patients with chronic diseases. The study's hypothesis is that in patients with chronic diseases, confinement leads to changes in health behaviors, non-adherence to pharmacological treatment and increased psychological stress leading to subsequent increased risk of deterioration in health status in short, medium, and long term.	Primary outcome: -% adherence to each pharmacological class (time frame: during the period from 20 April 2020 to 7 May 2020) -number of occurrence of medical events at 1 year (time frame: throughout the study for 12 months) Secondary outcome: -Non-pharmacological treatment/lifestyle, difficulties accessing care, and measurement of psychological distress: Kessler's specific questionnaire (score between 0 and 24): (time frame: during the period from 20 April 2020 to 7 May 2020)
113	Cardiovascular Prevention During COVID-19 Pandemic Lockdown in Young Adults (COLA Trial)/Brunner *et al.*/NCT04361877	Recruiting	Observational	1,900	The study aims to determine the impact of COVID-19 pandemic lockdown on cardiovascular prevention behaviour.	Primary outcome: Change of physical activity (time frame: 14 days) Secondary outcome: change in nutrition, semiquantitative change of alcohol intake, change of smoking behavior, change of stress level, step count
114	Integrated Distance Management Strategy for Patients With Cardiovascular Disease (Ischaemic Coronary Artery Disease, High Blood Pressure, Heart Failure) in the Context of the COVID-19 Pandemic/Burlacu *et al.*/NCT04325867	Recruiting	Interventional (clinical trial): intervention tested: telemedicine platform of remote monitoring through wearable devices	200	Given the Covid-19 pandemic, patients with complex cardiovascular conditions are under the obligation to stay in the house isolated and can no longer come to standard clinical and paraclinical monitoring and control visits. Therefore, a remote management solution (tele-medicine) of these patients must be found. The investigators aim to create an electronic platform to communicate with these patients and offer solutions for their cardiovascular health issues.	Primary outcome: -Providing a special electronic platform (e-health) for remote managing cardiovascular outpatients (time frame: 6 months) -number of patients included in this platform
115	A Telerehabilitation Approach to Improve Long-term Physical Ability and Quality of Life in Patients With Severe Acute Respiratory Syndrome Coronavirus (SARSCoV-2, COVID-19) Immediately After Hospitalization. The ATHLOS Study/Kortianou *et al.*/NCT04368845	Recruiting	Interventional (clinical trial): intervention tested: telerehabilitation device that includes breathing exercises and aerobic and resistance training exercises administered by a physiotherapist	100	The researchers test the efficacy of telerehabilitation by means of a device that includes breathing exercises and aerobic and resistance training exercises administered by a physiotherapist.	Primary outcome: -Physical Performance (time frame: Change From Baseline in SPPB Scores at 3 and 6 months) -Cardiorespiratory fitness -lower limb strength -health related quality of life -anxiety and depression -physical activity Secondary outcome: -fatigue -dyspnea
116	Does a Systematic Phone-call by a Medical Student/General Practitioner Team in Patients Suffering From a Chronic Condition During the COVID-19 Containment Period Impact One-month Hospitalization's Rate in France? A Cluster Randomized Trial/University Hospital, Tours/NCT04359875	Not yet recruiting	Interventional (clinical trial): intervention tested: behavioral-phone-call screening and management by a medical student/ general practitioner tandem	22,000	COVIQUEST project is cluster randomized trial designed to assess the optimizing of the screening and management of patients with chronic condition at risk of decompensation through a collaboration between the general practitioner and medical student. The goal is to assess the occurrence of hospitalization during a one-month period after a phone call in the setting of COVID-19 quarantine	Primary outcomes: -hospitalization(s) at one month (time frame: 1 month) Secondary outcomes: -phone call from general practitioner, mortality at one month, use of primary care and secondary care, number of prescriptions related to the chronic disease dispensed by the pharmacy, number of, time to, duration of, and reason for hospitalization, mortality at 6 months, cardiovascular events (MACE), psychotropic drugs

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Study number	Title/PI/NCT#	Status	Trial design	Estimated enrollment	Comments	Objective
117	The Heart Hive COVID-19 Study: A Longitudinal Observational Study of the Impact and Clinical Outcomes of the COVID-19 Pandemic on Individuals With Heart Muscle Disease/Ware *et al.*/NCT04468256	Not yet recruiting	Observational	1,000	The aim of this study is to conduct serial surveys in patients with cardiomyopathy and subjects without heart disease evaluating the health-related, behavioral and psychological impact of the COVID-19 pandemic, and to use national registries and medical records to longitudinally assess hospital admissions and patient mortality from COVID-19 for UK-based participants.	Primary outcomes: -qualitative measure of exposure, perception of risk, behavior, and experience during the COVID-19 pandemic (time frame: 2 years) -health outcomes
Other related studies						
118	CoronaWatch - Early Detection of Cardiovascular Risks in COVID-19 Via SmartWatch/Meder *et al.*/NCT04376853	Recruiting	Observational	50	Investigators aim to determine whether the addition of SmartWatches enhances risk stratification and early detection of complications and prognostics in patients with COVID-19 who have cardiovascular disease or receive medication with arrhythmogenic potential.	Primary outcome: -Biomarker (time frame: 3 months) -Identification of biomarkers (laboratory-chemical, clinical, digital) for risk stratification and early detection of complications and prognosis
119	Multi-Center Prospective Cohort Study: Impact of Burnout on Cardiovascular and Immune Biomarkers Among Frontline Healthcare Professionals During Covid-19 Pandemic in Abu Dhabi Emirate/Almahmeed *et al.*/NCT04422418	Recruiting	Observational	200	The objective of this study is to investigate the evolution of psychological, cardiovascular, and immune markers in healthcare professionals with different levels of exposure to the COVID-19 pandemic. These markers will be stratified by the level of exposure to the COVID-19 pandemic, positive diagnosis of COVID-19, profession, sex, age, and already existing cardiovascular risk	Secondary outcomes: -Change from baseline -Cardiovascular risk through heart rate variability markers at 2-3 months and 6 months (time frame: baseline, 2-3 months, 6 months) -Data is collected through wearable monitoring technology
120	Robot Assisted Percutaneous Cardiovascular Intervention as a Strategy to Reduce or Risk of Intra-Procedure Contamination by COVID-19 and Other Respiratory Viruses/Lemos *et al.*/NCT04379453	Recruiting	Interventional (clinical trial): intervention tested: robot assisted percutaneous cardiovascular intervention	10	COVID-19 pandemic increased the interest in performing procedures with robotic assistance. This allows timely intervention without exposing physicians or patients to transmission of airborne infections.	Primary outcomes: -Successful cardiovascular intervention (time frame: Until the end of the procedure) -Performed with the professional team positioned at > 2 meters from the patient for at least 50% of the duration of the intervention -absence of fatal complications caused by the procedure or acute non-fatal vessel occlusion during index admission
121	Stain Therapy and COVID-19 Infection (STACOV Project) /Masana *et al.*/NCT04407273	Recruiting	Observational	1,200	Considering that stains interfere with SARS-CoV-2 cellular uptake and some inflammatory pathways activated by the virus, the researchers hypothesize that patients on statin therapy should be less vulnerable to infection and their clinical course and prognosis potentially better than individuals not on statin therapy.	Primary outcome: -SARS-CoV-2 scale of severity (9 steps) in COVID-19 infected patients with statin therapy (time frame: at the time of admission)
122	International Study on Acute Coronary Syndromes - ST-segment Elevation Myocardial Infarction COVID 19/Università degli Studi del Piemonte Orientale "Amedeo Avogadro"/NCT04412655	Active, not recruiting	Observational	6,609	This is a retrospective multicenter registry study aimed at estimating the real impact of COVID-19 pandemic on treatment and outcome of STEMI by primary angioplasty, and to identify risk factors for delays in interventions or deferral in seeking treatment.	Primary outcome: -Number of patients undergoing primary angioplasty (time frame: March April 2019 and 2020) -Number of patients undergoing primary angioplasty later than 12 hours from symptoms onset; -Number of patients undergoing primary angioplasty later than 30 minutes from PCI hospital admission -In-hospital mortality

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