BJGH Brazilian Journal of Global Health
Revista Brasileira de Saúde Global

Clinical cardiological predictors in the COVID-19 pandemic: an integrative review

Victoria Reimberg[1*], Sérgio Henrique Simonetti[1], Li Men Zhao[1]

[1]Instituto Dante Pazzanese de Cardiologia (IDPC).

ABSTRACT

OBJECTIVE

COVID-19, caused by severe acute respiratory syndrome (SARS-Cov-2), started in China, in the *Hubei* province, triggering a pandemic. Prognostic factors or clinical predictors are characteristics that can be used to predict the progression of the disease and the way in which chronic comorbidities can influence the poor prognosis of affected patients who are then infected by the new coronavirus. The aim of the present study was to analyze the clinical predictors in the literature in patients with heart disease infected by COVID-19.

METHODS

This is an integrative literature review study. To elaborate the guiding question, the method used was the PVO strategy, where P (*population*) is the cardiac patients infected by COVID-19, the V (*variable*) is the variable of interest, which in this study will be the clinical predictors during the infection, and finally the O (*outcome*) consists of the results, that is, the prognosis and clinical manifestations. The research was carried out in the Virtual Health Library (VHL) and at *PUBMED*.

RESULTS

The initial search resulted in 228 articles. Using the PRISMA tool, 37 articles were selected for the partial sample. The final sample consisted of 27 original articles published in English, Spanish, and Portuguese. The selected publications were subjected to thematic analysis, separated and grouped into five categories: laboratory alterations, imaging tests, continuous use medications, comorbidities, and electrocardiographic alterations.

CONCLUSIONS

The relationship between the cardiovascular system and the Coronavirus infection is evident in several studies, as well as that this association leads to more serious outcomes for heart patients.

DESCRIPTORS

Heart diseases, Coronavirus infection, Prognosis, Risk Factors.

Corresponding author:
Victoria Reimberg.
Residente em Enfermagem Cardiovascular no Instituto Dante Pazzanese de Cardiologia (IDPC). Av. Dr. Dante Pazzanese, 500 - Vila Mariana, São Paulo – SP, Brasil.
E-mail: victoria.reimberg@dantepazzanese.org.br
ORCID ID: http://orcid.org/0000-0003-2386-0364

INTRODUCTION

In December 2019, a new disease began in the world, that would trigger an outbreak, followed by a pandemic.(1) COVID-19, caused by severe acute respiratory syndrome (SARS-Cov-2), through coronavirus infection, began in China, in the Hubei province and despite the hypothesis that it started as a zoonotic transmission by commercialization of wild animals, community transmission has ensued[1,2].

The first case of coronavirus infection notified to the Ministry of Health in Brazil was on February 26, 2020 and, since then, health systems have undergone several changes to adapt to the high demand for care[3]. The disease has spread devastatingly around the world, bringing social impacts, especially for health due to the overload of care systems for patients infected by the new virus[3,4].

Patients diagnosed with COVID-19 may present symptoms of flu-like syndromes such as: cough, dyspnea, runny nose, and headache, and, in addition, other systemic manifestations can be observed in these individuals, especially in those who already have a primary diagnosis, such as underlying diseases (hypertension, diabetes)[5]. In addition to respiratory alterations, the cardiovascular system has been one of the most affected[5,6].

According to the Brazilian Society of Cardiology[7], infection with the new coronavirus can affect the cardiovascular system and potentiate existing symptoms in patients with some type of heart disease[6,7]. The main manifestations are arrhythmia (16%), myocardial ischemia (10%), myocarditis (7.2%), and shock (1-2%). Thus, intensifying care in the population with cardiovascular diseases is essential for the best prognosis in case of infection by the new coronavirus[6,7]. To this end, it is necessary to know the conditions that can worsen the prognosis and the best form of treatment available[6,7].

Pre-existing risk factors or clinical predictors are patient characteristics that can be used to predict the progression of the disease[8]. These factors may be indicative of the patient's clinical course while hospitalized during the period of infection[9]. When studied, these factors guarantee the analysis of the severity of the disease according to its evolution, allowing the early implementation of the best therapy and treatment [8,9].

According to data from the *American College of Cardiology* (ACC), chronic diseases such as hypertension, diabetes, and coronary artery disease can influence the poor prognosis of patients who have these comorbidities and are infected by the new coronavirus[10].

In view of the above, it appears that it is essential to know the main clinical predictors in patients with heart disease infected with the new coronavirus and how they can be determining prognostic factors in the clinical evolution during the period of infection.

Thus, the objective of the current study was to analyze the scientific literature with respect to the main alterations that are clinical predictors of unfavorable evolution in patients with heart disease infected by COVID-19, in addition to identifying and correlating these risk factors with unfavorable outcomes in patients with heart disease.

METHODS

This is an integrative literature review study using methods and criteria defined from a guiding question, through search, extraction, analysis, and discussion of data[11].

An integrative review provides a synthesis of the subjects to be studied, and the incorporation and practical applicability of the results found. To structure the research, the six basic steps of an integrative review were followed[12].

The first step was to formulate the problem or guiding question, aiming to determine which studies would be included and which methods would be adopted to collect the data[12]. Based on the relevance identified in the subject, the guiding question of this study was formed: Which clinical predictors presented in heart disease patients infected by coronavirus affect the prognosis?

To elaborate the guiding question, the method used was the PVO strategy[13], where P (*population*) is patients with heart disease infected by COVID-19, V (*variable*) is the variable of interest, which, in this study, will be the clinical predictors of these patients during infection, and the O (*outcome*) consists of the results, that is, the prognosis and clinical manifestations[13,14].

After defining the guiding question, the inclusion criteria were defined in the study, which are full articles, published in Portuguese and English, that addressed the topic proposed by this integrative review, found in the aforementioned databases, in the period 2020 to 2021.

The exclusion criteria established were duplicate articles, research carried out with pediatric and pregnant patients, incomplete articles, case reports, and meta-analyses.

Table 1. Construction of the guiding question through the PVO strategy

Strategy Items	Components	Subject Descriptors (DeCS)	Key-words
Population	Patients with heart disease infected by COVID-19	Cardiopathies	Cardiac diseases; Heart disease
Variables	Clinical Predictors	Coronavirus infection	COVID-19
Outcomes	Clinical Manifestations	Prognosis	Prognostic Factors

Source: authorial, 2021

Within the PVO, the prognostic factors are alterations in laboratory tests, cardiac biomarkers, and markers of inflammatory response, in addition to changes in imaging tests. On the other hand, the clinical manifestations are characterized as the outcomes presented by the individuals in the studies.

The second step consists of a broad literature search, carried out in electronic databases, to check that the data used in the research met the previously defined inclusion criteria[12].

Data from this research were collected from electronic databases: Latin American and Caribbean Literature on Health Sciences (LILACS), Nursing Databases (BDENF), Medical Literature Analysis and Retrieval System Online (Medline), PUBMED Central (PMC), and the Virtual Health Library (BVS), from December 2020 to March 2021, with the truncation of the descriptors Cardiopathies, Coronavirus infection, and prognosis by the Boolean operator AND.

The articles found were input to in EndNote Web Basic (Clarivate Analytics ®) for organization and better selection of data.

To aid in the process of selection and reporting of the integrative review, the PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) recommendation was used, which is a tool to support rigor when verifying the quality criteria of a study[12,15].

The third step followed with the evaluation of the data. At this stage, the findings obtained from the articles were carefully extracted to ensure that they were used reliably and that they answered the guiding question of the project[12].

Data analysis started in the fourth stage by organizing the data found and classifying the level of evidence of each study, based on the methodological approach of each one[12].

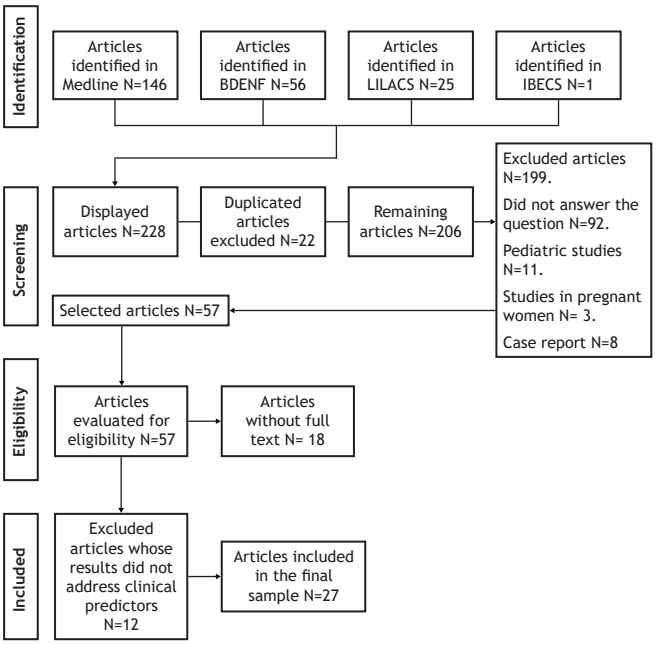
In the fifth stage, the discussion of the results was carried out. From this stage, the results began to be interpreted and synthesized, presenting the opinions and conclusions about the data obtained[12].

In the final step, the presentation of the review was carried out in a clear way, containing the information worked in a complete way, based on the methodologies used[12].

RESULTS

The search carried out in the databases resulted in 228 publications. After selection according to the eligibility criteria, a final sample of 27 articles was included, as illustrated in Figure 1.

Figure 1. PRISMA flowchart referring to the article search and selection process.

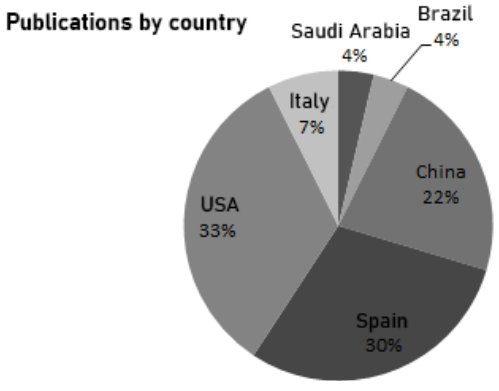


Source: authorial, 2021

Of the entire sample, 16 articles were identified in MEDLINE, five in BDENF, five in LILACS, and one in IBECS.

Regarding geographic distribution, the United States of America (USA) had more publications on the subject (33.3%) with nine articles, followed by Spain (eight articles), China (six articles), Italy (two articles), and Saudi Arabia and Brazil (both with one article), as shown in Figure 2. Regarding the language of publication, English was prevalent (18 articles), followed by Spanish (8 articles) and Portuguese (1 article).

Figure 2. Distribution of articles by place of origin of the study. N=27 articles.



Source: authorial, 2021

Table 2 presents the synthesis of the articles selected for the final sample of the study to facilitate the understanding and schematization of the information obtained.

Table 2. Synthesis of studies according to authorship, year, and place of publication and study design. N= 27 articles. São Paulo-SP, 2022.

N°	Year and Country	Author (s)	Study design
1	2020, China	Chen Chen[23]	Review study
2	2020, Spain	Esther Guerrero Pérez[29]	Review study
3	2020, United States	Chirag Bavishia[19]	Review of clinical trials
4	2020, United States	Aws Almufleh[16]	Retrospective study
5	2020, New York	Sripal Bangalor[17]	Retrospective study
6	2020, Spain	Estefanía Cantador[21]	Retrospective study
7	2020, China	Liang Cao[22]	Retrospective study
8	2020, New York	Jason S. Chinitz[24]	Retrospective study
9	2020, Spain	Alfredo Bardají[18]	Retrospective observational study
10	2020, Spain	Ana Pardo Sanz[36]	Retrospective observational study
11	2020, Italy	Alessandro Mengozzi[35]	Prospective observational study
12	2020, United States	Mohamad Raad[38]	Retrospective longitudinal cohort study
13	2020, Italy	Francesca Bursi[20]	Retrospective cohort study
14	2020, United States	Orly Efros[25]	Retrospective cohort study
15	2020, United States	Pierre Elias[26]	Retrospective cohort study
16	2020, Spain	Rafael Golpe[28]	Retrospective cohort study
17	2020, Saudi Arabia	Anas Khan[31]	Retrospective cohort study
18	2020, China	Junli Li[32]	Retrospective cohort study
19	2020, Spain	Diego López-Otero[33]	Retrospective cohort study
20	2020, China	Xiaojun Ma[34]	Retrospective cohort study
21	2020, Spain	Juan R. Rey[39]	Retrospective cohort study
22	2020, Spain	Weifeng Shang[40]	Retrospective cohort study
23	2020, China	Daoyuan Si[41]	Retrospective cohort study
24	2020, China	Huayan Xu[42]	Retrospective cohort study
25	2020, Brazil	Vanessa Cristine[27]	Cross-sectional descriptive study
26	2020, United States	Anas Hamadeh[30]	Multicenter retrospective study
27	2020, United States	Juan-Juan Qin[37]	Multicenter retrospective study

Source: authorial, 2021

Table 3 presents the articles selected for this review, listing research participants and the main conclusions of the study.

Table 3. Summary of research participants and main conclusions of the studies. N= 27 articles. São Paulo-SP, 2022.

N°	Research Participants	Study Conclusion
1	21 subjects treated at the institution before the pandemic, followed remotely for 57 days post-infection for monitoring of pulmonary artery pressure (PAP)	Effective remote management of patients with heart disease on an outpatient basis showed no clinical impairment, even for those with increased pulmonary artery pressure.
2	18 individuals with confirmed Covid-19 and ST-segment elevation on electrocardiography or who had non-obstructive coronary disease	Both obstructive and non-obstructive disease were poor prognostic factors. All subjects had elevated levels of D-Dimer. Of the 18 patients, 13 died during hospitalization due to COVID -19.
3	433 subjects treated for suspected or confirmed SARS-CoV-2 who had at least 1 cardiac troponin I measurement	Cardiac troponin was a marker of poor prognosis for both the confirmed COVID-19 group and the excluded group, however, mortality was higher in the confirmed COVID-19 group.
4	-	Sample of 11685. Cardiac biomarkers can be used to aid in diagnosis as well as risk stratification.
5	49 individuals diagnosed with COVID-19 undergoing an echocardiographic examination	Longitudinal deformation of the RV was a predictor of mortality. Predominant RV dysfunction may represent the final common pathway related to COVID-19 prognosis.
6	1419 Individuals with COVID-19 and clinically suspected acute cerebral, coronary, or peripheral vascular events	COVID-19 may favor the occurrence of thrombotic events, however, the destabilization and thrombosis of atherosclerotic plaques does not seem to be a frequent mechanism that justifies the need for specific systematic preventive measures.

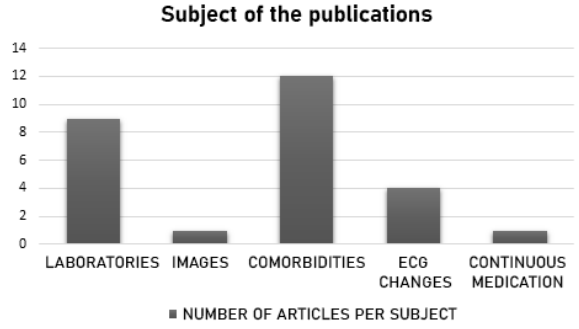
7	100 individuals with severe COVID-19 analyzed through clinical and laboratory findings	Myocardial injury evidenced by elevation of biomarkers associated with COVID-19 had a poor prognosis. The increase in troponin indicates myocardial damage and is associated with disease severity.
8	-	Elevated NT-pro BNP and troponin were higher in critical COVID-19 cases than in mild COVID-19 cases. Both were correlated with critical illness status.
9	Seven individuals with confirmed COVID-19 who required pacing support for severe bradycardia	Acute bradycardia was associated with elevated inflammatory markers and high short-term mortality rates, even in the absence of coexisting cardiomyopathy or acute cardiac injury.
10	559 individuals diagnosed with COVID-19 and at least one high-sensitivity troponin assay within 24 hours of admission	Elevated troponin levels were associated with reduced survival and increased risk of the invasive ventilatory support outcome and death. It was also associated with an increased risk of other in-hospital events, such as acute kidney injury and low oxygen saturation.
11	1,258 adults with coronavirus disease 2019 who had an electrocardiogram presentation	Abnormal respiratory vital signs and ECG with the presence of atrial flutter/fibrillation, right ventricular overload, or ST-segment abnormality were poor prognostic factors. More patients are intubated within the first 24 hours after presentation of these characteristics.
12	Deaths confirmed from Covid-19 in the State of Paraná	Within the profile of deaths, we observed higher mortality in older men (67% over 60 years old) (67%), the most common associated conditions were hypertension (23%), diabetes (21%), and heart disease (13%).
13	539 hypertensive individuals diagnosed with SARS-CoV-2 infection	ACE inhibitors and ARBs were not linked to an increased risk of having COVID-19 or a more severe form of the disease. ACE inhibitor treatment was associated with a lower risk of mortality in hospitalized cases.
14	-	The increase in basal renin in patients with heart disease infected by COVID-19 is related to a worse prognosis due to overexpression of angiotensin II converting enzyme.
15	78 individuals hospitalized with COVID-19 infection and ST-segment elevation	Of the 78 patients with STEMI and COVID-19 infection, 14 (18%) required invasive MV. COVID-19 infection and the systemic inflammatory response can be a trigger for a STEMI event.
16	648 confirmed COVID-19 cases with definitive outcomes in Saudi Arabia during March 2020	Risk factors associated with worse outcomes included men, age >60 years, heart disease, chronic respiratory disease, and cases with two or more comorbidities.
17	74 severe or critical COVID-19 individuals at Wuhan Fourth Hospital between January 25 and February 26, 2020	Older males with chronic diseases have a higher risk of death. Lymphopenia, neutrophilia, elevated CRP, and procalcitonin were factors of worse prognosis among critically ill individuals.
18	245 individuals with confirmed SARS-CoV-2 infection in our healthcare area who were admitted to hospital	Elevated troponin in subjects without heart disease indicated more severe infection and respiratory distress. In individuals with previous heart disease, troponin elevation may not only be related to the infectious process, but also to the underlying disease, so that, by itself, it does not identify the severity of COVID-19.
19	262 individuals diagnosed with COVID-19 and hospitalized in China from January 12, 2020 to March 20, 2020	Platelets and D-dimer were independent risk factors for predicting outcome in COVID-19 patients. In addition, lymphocytes, lactate, and CRP were also risk factors that affected the patient's prognosis.
20	266 consecutive individuals hospitalized for SARS-CoV-2 pneumonia at the university hospital	Elevated CRP was related to the risk of ICU admission and need for MV, however, it was not predictive of mortality. D-dimer and troponin showed a strong relationship with mortality.
21	160 hospitalized individuals with COVID-19 infection with recent-onset AF and patients in sinus rhythm or hospitalized with previous AF	New-onset AF in the context of COVID-19 disease has a worse prognosis and a higher incidence of embolic events and of bleeding events.
22	3,219 individuals diagnosed with COVID-19 hospitalized to estimate the prognostic power of cardiac injury markers	Elevations of biomarkers such as troponin, CK-MB, (NT-pro)BNP, or Myoglobin were highly predictive of all-cause mortality at 28 days, including deaths occurring shortly after admission. In addition, the elevation of these biomarkers was also associated with more severe symptoms and disease progression.
23	1,044 individuals consecutively admitted with COVID-19 from March 9 to April 15	Cardiovascular risk factors and cardiovascular diseases led to an increased risk of developing cardiac injury. Cardiac injury was associated with a higher risk of intensive care unit admission, mechanical ventilation support, and mortality.
24	3,080 consecutive individuals with confirmed COVID-19 infection and at least 30-day follow-up	Individuals with COVID-19 have a significant incidence of acute HF, which is associated with poor outcomes and a worse clinical framework at first medical contact, with higher all-cause mortality.
25	443 hospitalized individuals with COVID-19 analyzed retrospectively, divided into non-severe and severe group.	The increase in the ratio of neutrophils to lymphocytes and CRP together with the decrease in platelet count were factors of worse prognosis.
26	1,284 subjects with severe COVID-19 with a measurement of troponin level at hospital admission	Initial troponin levels were associated with poor survival, and its peak was a predictor of ventilatory support. In addition, cardiac arrhythmias were reported in up to 16% of individuals and an even higher frequency (44.4%) among ICU patients.
27	102 consecutive laboratory-confirmed and hospitalized individuals with COVID-19	Tachycardia, high levels of myocardial enzymes and cardiac dysfunction were prognostic factors for a worse outcome. CRP levels, advanced age, pneumonia severity, and comorbidities were the main risk factors for acute cardiac injury in patients with COVID-19.

Source: authorial, 2021

After reading the articles in full, they were separated and grouped into five thematic categories: laboratory alterations, imaging tests, continuous use medications, comorbidities, and electrocardiographic alterations.

The *Comorbidities* axis was the most commonly found subject in the literature, with a total of 12 publications, *Laboratory Examinations* with a total of nine articles, followed by *Electrocardiographic Alterations* with four articles, and *Imaging Examinations* and *Continuous Medication*, both with one article, as shown in Graph 1.

Graph 1. Distribution of publications by thematic axis. N= 27 articles. São Paulo-SP, 2022.



Source: authorial, 2021

DISCUSSION

Addressing the issue of COVID-19 has been a major challenge in the health area, especially when related to the cardiovascular system and the complications that can have repercussions, especially because the symptoms of the infection are not always respiratory in nature. The present study sought to present a sample of infected patients with heart disease who presented laboratory and clinical alterations that could possibly be used to predict the course of the disease[16].

Since the beginning of the pandemic, it has been noted that, among those infected by the virus, individuals who acquired the most severe form of the disease were of advanced age or had a pre-existing comorbidity. A cross-sectional study[27] carried out in Paraná showed that the clinical conditions associated with deaths from COVID were hypertension (23%), diabetes

mellitus (21.8%), and previous heart disease (13.6%). In addition, modifiable risk factors for cardiovascular disease such as obesity, alcohol consumption and smoking were also present[27]. The predominance of deaths among older people can be explained by the greater lethality of the disease in this population, since they have more comorbidities. Cases aged 65 years or older showed a higher risk of hospitalization in intensive care units, in addition to the death outcome[31].

Another comorbidity associated with worse prognosis was chronic heart failure (CHF). Considering that heart failure is one of the main causes of mortality in the world, its association with COVID-19 infection has brought serious harm to infected patients. A study of 152 patients with CHF and a confirmed COVID-19 infection[39] reported a lower glomerular filtration rate in these patients, in addition to a decrease in hemoglobin. The patients presented clinical manifestations of acute heart failure (AHF), evidenced by increased ventricular dysfunction and elevation of cardiac biomarkers. Myocardial alterations evidenced in these patients are related to higher mortality and acute decompensation[39].

Cardiac injury was also a relevant factor to indicate worse outcomes in infected patients. This fact can be taken into account, since heart muscle injury can potentiate the severity of COVID-19 infection. The virus can directly affect the myocardium through viral toxicity in cardiomyocytes or through the formation of microthrombi in the venous network, leading to microvascular dysfunction. There is also a difference in oxygen supply and demand due to acute myocardial infarction (AMI) in patients with previous coronary artery disease. In all scenarios, there is myocardial suffering that can lead to hemodynamic alterations, resulting in worse outcomes[42]. It was observed that the clinical course of patients with myocardial injury affected by COVID-19 was unfavorable. Among the outcomes are severe forms of the disease, ICU admission, and death[23,42].

Among the laboratory alterations, cardiac troponin, a marker of myocardial injury, was the most prevalent in the articles raised on the subject. Its prognostic implications are seen in patients with COVID-19 infection. A study carried out with 1795 patients[18] showed that hospital mortality was 18.8%, and of these, 53.7% had elevated troponin levels, evidencing myocardial injury. Detecting this lesion through troponin elevation can aid in decision making about ICU admission and in therapeutic proposals, however, the study revealed that the predictive capacity of elevated troponin was the same in patients infected by the virus and those who were not, although mortality was higher in the confirmed group[18]. On the other hand, troponin was also considered an independent prognostic factor for critically ill patients with COVID-19, that is, it was used to predict the course of the disease in patients with myocardial injury and that these would have an unfavorable prognosis[18, 22].

Another relevant fact is that the rapid increase in troponin from the 16th day after the onset of symptoms of infection was prevalent in non-survivors. For this reason, troponin measurement was adopted as a routine laboratory test for monitoring during hospitalization to assist in the early identification of myocardial injury and worse prognosis[19].

The recommendation of laboratory measurement of troponin in patients infected with COVID-19 is essential for the diagnosis of myocarditis, stress-induced cardiomyopathy, and AMI. Several health societies have recommended troponin dosing during the pandemic in different contexts. The *Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment*[25] recommends its use in all patients with the infection. The World Health Organization (WHO) recommends the use of troponin for the clinical management of severe acute respiratory infection, even in suspected cases. The *American College of Cardiology* indicates troponin dosage only in cases of a suspected AMI diagnosis[25].

An analysis carried out with 245 patients with confirmed COVID-19 infection showed that major events occurred in both patients with previous heart disease and in those with no history. In all cases, the elevation in troponin was related to higher mortality, however, it was not a predictor of the development of heart failure. Patients with no prior history of heart disease and with troponin elevation exhibited the infection in its most severe form, showing greater specificity to determine the prognosis of COVID-19. The elevation of this biomarker in patients with previous heart disease was not specific to predict the course of the disease, since it could be associated not only with the infectious process, but also with the underlying disease[33].

In a study carried out in Italy[35], troponin dosage was shown to be superior to predict the course of COVID-19 infection when compared to other biomarkers. The elevation in troponin was five times greater in individuals who died than in patients who survived during the hospital stay[35]. In addition, the study showed that the association of troponin with other inflammatory markers, such as CRP and D-dimer showed a strong correlation with the indication of a worse prognosis. This fact may be related to the oxytocin storm and the inflammatory process during the period of infection[33,35].

The inflammatory process triggered by COVID-19 infection is closely linked to cardiac injury, evidenced by the increase in troponin. However, other biomarkers were also used to show myocardial damage in patients during the period of contamination, in addition to helping to predict the course of the disease. Elevation of cardiac biomarkers such as CK-MB (Creatine kinase-MB), CK (Creatine kinase), BNP (B-type natriuretic peptide), and Myoglobin was associated with increased mortality and was clinically significant for monitoring these patients to provide better interventions during hospitalization. In a sample of patients, specific cardiac biomarkers (troponin, CK-MB, and BNP) showed greater sensitivity to estimate cardiac injury [37].

In addition to indicating the prognosis of cardiovascular disease in patients with COVID-19, biomarkers have also been instrumental in aiding clinical interventions during the course of the disease. A retrospective cohort study conducted in the USA[38] showed that the cardiac injury demonstrated by elevated cardiac biomarkers at the time of admission was also associated with a strong need for mechanical ventilation in these patients[38]. In addition to the need for mechanical ventilation, worse prognosis and the death outcome were predicted by the elevation in cardiac biomarkers, and these were also associated with more severe symptoms, demonstrating the importance of early dosage to help the team in clinical decision making[37].

The use of laboratory tests proved to be crucial for the assessment of factors that affect the progression of heart disease in patients with COVID-19. A study that evaluated the relationship between clinical indices and disease severity compared laboratory tests at admission of critically ill and non-severe patients. The results showed that the elevation of the NRL, a marker of the inflammatory process, was much higher in the group of critically ill patients. In addition to this marker, CRP (C-reactive protein) was also significantly higher and was an independent factor in predicting the most aggressive form of the disease and its outcome. Patients who had the outcome of death presented significant thrombocytopenia when compared to another group[40]. Elevated CRP may be related to persistent inflammatory responses in patients with COVID-19 and, in more severe cases, this process occurs more intensely, which can lead to tissue damage and myocardial injury, as evidenced in the aforementioned studies[34].

A study that exhibited clinical laboratory parameters of 74 patients at hospital admission showed that 71.6% presented lymphopenia, 70.2% presented increased neutrophil counts, and 93.2% presented elevated CRP. These data reveal the severity of the patients, indicating an exacerbated inflammatory

process, in addition to a higher incidence of cardiac injury. Therefore, use of the dosage of inflammatory markers is recommended to assess the risk of diseases in these patients[32].

Another important biomarker in the prognosis of patients with heart disease affected by COVID-19 was D-dimer, which is a product of fibrin degradation, being used as a thrombotic marker. A case series of 18 patients showed that, during hospitalization for COVID-19, all presented D-dimer elevation, and, among these patients, all had myocardial injury. These data show the importance of dosing and monitoring D-Dimer as an adjuvant in clinical decision-making and determining the prognosis of patients during the hospitalization period[17]. A nomographic model, based on clinical and laboratory parameters, used to predict the survival of patients with COVID-19 showed that D-Dimer dosage was an independent risk factor for prognosticating patients with a greater chance of developing the severe form of the disease and was included in the nomographic model to predict the course of infection, demonstrating its relevance in clinical practice during hospitalization[34].

Knowing the prognostic relevance of D-Dimer in individuals with COVID-19 to predict thrombotic events, a study carried out with 1419 patients in Spain showed strong evidence of thrombosis cases in these patients, however, a 1% incidence of systemic arterial events was observed with a mortality rate of 28.6%. One of the limitations of this study was the underestimation of sudden death cases. These data open space for further research in order to identify possible gaps on the subject[21].

Currently, it is understood that COVID-19, associated with heart disease, has a worse prognosis for patients with this condition, including a higher mortality rate. It was noted that these individuals are more vulnerable to the pathophysiological mechanism of Coronavirus due to the elevation in renin, which is related to a higher prevalence of heart failure. The increase in basal renin is related to a worse prognosis, since, in excess, it causes increased expression of angiotensin-converting enzyme (ACE), responsible for converting angiotensin II into angiotensin I, triggering a marked effect of bradykinin and leading to imminent clinical worsening. Therefore, the basal renin measurement can also be used as a laboratory supplement in patients with the characteristics described[29].

Electrocardiographic alterations were frequently evidenced in patients diagnosed with COVID-19. A case report with seven patients performed in New York[24] showed that severe bradycardia was present at the time of hospital admission, with three symptomatic and four asymptomatic cases. During hospitalization, all patients received stimulation with a permanent or temporary pacemaker implant, however, after three months, five out of seven patients died from complications resulting from the viral infection. Data such as these show the relationship between the virus and arrhythmias which can be explained by the mechanism of viral infiltration in myocardial cells, impairing the cardiac conduction system. No patient in this sample presented an ischemic alteration on the ECG and the mortality rate was considered high in the short term[24].

In other studies, ST-segment elevation was considered important to aid in the prognosis of patients infected with COVID-19. A cohort of 1258 subjects in the United States analyzed 850 ECGs at hospital admission of patients with COVID-19. The presence of electrocardiogram abnormalities, especially ST-segment elevation evidenced in 812 patients, was highly prognostic at 48 hours. The main outcomes include the need for mechanical ventilation and death[26].

A study carried out with a total of 78 patients infected with COVID-19 who had ST-segment elevation on the ECG showed that 18% required invasive mechanical ventilation during hospitalization. Of all the patients, 19 were treated with percutaneous coronary intervention (PCI) and 59 with fibrinolytic therapy, however, despite the different reperfusion strategies, the overall mortality rate was 12%. The data show the correlation of COVID-19 and acute myocardial infarction, demonstrating that the thrombotic complications triggered by the infection can be a clinical predictor to aid in the treatment in cases like this[30].

Another electrocardiographic alteration that presented prognostic relevance was the presence of Atrial Fibrillation (AF) and Atrial Flutter. An observational study that analyzed 160 hospitalized patients with COVID-19 showed that the group with recent-onset AF presented a higher number of embolic events during hospitalization, in addition to thrombosis outcomes and longer hospital stays. This relationship is due to the fact that AF is an independent predictor of embolic events which is potentiated during viral infection[36]. Atrial flutter was also considered a marker of poor prognosis in patients with COVID-19, evidencing that patients with this ECG alteration had early intubation during the first 24 hours of hospitalization and was associated with higher 48-hour mortality. The clotting disorder evidenced in COVID-19 cases stands out as a risk factor for embolic events, in addition to which, atrial arrhythmias can increase the chance of thrombus formation[26]. There are reports that cardiac arrhythmias were evidenced in 16% of patients infected with COVID-19 during hospitalization and in 44% of ICU patients. This reinforces the correlation of the presence of conduction disturbances on the ECG with the severity of the infection during hospitalization[41].

Other important data used as a clinical predictor during the COVID-19 pandemic were echocardiogram characteristics. A survey carried out in Milan showed that longitudinal deformation of the right ventricle (RV) was an independent predictor of mortality in patients with heart disease infected with COVID-19, as evidenced by transthoracic echocardiography. These findings are important for decision making that may impact the prognosis of these patients[20].

At the beginning of the pandemic, there was an expert discussion on whether angiotensin-converting enzyme (ACE) inhibitor drugs or angiotensin II type I receptor blockers (ARB) could increase the risk of COVID-19. A cohort study evaluated patients with COVID-19-infected hypertension showed that the use of these drugs is not associated with a worse clinical outcome in these patients. ARB was also associated with a lower risk of hospital admission and treatment with ACE inhibitors was associated with a lower risk of mortality[28].

CONCLUSION

Through the analysis of the studies, it was possible to observe that both clinical and laboratory predictors are of paramount importance to aid in the prognosis of patients with heart disease who are infected by COVID-19. In addition to predicting the course of the disease, the data can help in clinical decision making in order to obtain better outcomes that improve nursing care for cardiac patients.

In this study, the cardiovascular clinical predictors for COVID-19 infection stand out; the male sex, age > 60 years, heart diseases, severity of pneumonia and chronic respiratory diseases, hypertension, diabetes, and heart disease were determinants for acute cardiac injury. The study also considered, through the studies identified, whether drug treatment with ACE inhibitors and ARBs, the profile of patients with STEMI, and with high levels of platelets, CRP and D-dimer, CK-MB, or myoglobin, myocardial markers (NT-proBNP and cardiac troponin), as well as lymphopenia, neutrophilia, elevated CRP, and procalcitonin were factors of worse prognosis.

The results also considered that the significant incidence of acute HF, which is associated with poor results and clinical framework, and the initial levels of troponin were associated with decreased survival, and its peak was a predictor of ventilatory support. In addition, cardiac arrhythmias were reported

in the studies presented in this study.

The increase in the ratio of neutrophils to lymphocytes and CRP together with the decrease in platelet count were factors for a worse prognosis. AF had a worse prognosis and a higher incidence of embolic events and of hemorrhagic events. On the other hand, cardiac injury and longitudinal deformation of the RV, and acute bradycardia associated with an increase in inflammatory markers were determinant for the poor prognosis of patients with these profiles.

Elevated troponin levels were associated with reduced survival, the increased risk of invasive ventilatory support outcome and death. Acute kidney injury and low oxygen saturation, abnormal respiratory vital signs and ECG with the presence of atrial flutter/fibrillation, right ventricular overload or ST-segment abnormality were poor prognostic factors for COVID-19 infection.

Through clinical predictors, it is possible to define the course of infection to determine the best interventions and behaviors, aiming at the recovery and rehabilitation of individuals with heart disease who are infected by Coronavirus.

Coronavirus is characterized as a new disease in the medical context, which makes it difficult to define interventions and treatment for the population addressed in this review. This difficulty brings limitations to the study, as further research is needed to improve therapeutic measures related to COVID-19.

REFERENCES

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020;395(10229):1054-62.
2. Félix-Oliveira A, de Sousa Almeida M, Ferreira J, Campante Teles R, Mesquita Gabriel H, Cavaco D, et al. Caring for cardiac patients amidst the SARS-CoV-2 pandemic: The scrambled pieces of the puzzle. Rev Port Cardiol. 2020;39(5):299-301.
3. Ministério da Saúde Secretaria de Vigilância em Saúde Doença pelo Coronavírus COVID-19 BOLETIM EPIDEMIOLÓGICO ESPECIAL. Brasil, 2021.
4. Estrela FM, Soares CFSe, Cruz MAd, Silva AFd, Santos JRL, Moreira TMdO, et al. Pandemia da COVID-19: refletindo as vulnerabilidades a luz do gênero, raça e classe. Ciência & Saúde Coletiva. 2020;25:3431-6.
5. Martins J, Melo Sardinha D, Silva R, Lima K, Lima L. As implicações da COVID-19 no sistema cardiovascular: prognóstico e intercorrências. Journal of Health & Biological Sciences. 2020;8:1.
6. Askin L, Tanr1verdi O, Askin HS. O Efeito da Doença de Coronavírus 2019 nas Doenças Cardiovasculares. Arquivos Brasileiros de Cardiologia. 2020;114:817-22.
7. Sociedade Brasileira de Cardiologia. Nota de esclarecimento. Infecção pelo Coronavírus 2019 (COVID-19). São Paulo (SP); 2020.
8. Stafin I, Caponi LGF, de Araujo JN, Torres TP, Guedes VR. Fatores prognósticos no câncer de mama. HU Revista. 2014;38(3 e 4).
9. George SL. Identification and assessment of prognostic factors.Semin Oncol. 1988 Oct;15(5):462- 71.
10. Rente A, Uezato Junior D, Uezato KMK. Coronavírus e o Coração Um Relato de Caso sobre a Evolução da COVID-19 Associado à Evolução Cardiológica. Arquivos Brasileiros de Cardiologia. 2020;114:839-42.
11. Souza MTd, Silva MDd, Carvalho Rd. Integrative review: what is it? How to do it? Einstein (São Paulo). 2010;8:102-6.
12. Galvão MCB, Ricarte ILM. Revisão Sistemática Da Literatura: Conceituação, Produção E Publicação. Logeion: Filosofia da Informação. 2019;6(1):57-73.
13. Alves MJH, Pereira EV, Belém JM, Quirino GdS, Maia ER, Alencar AMPG. Fatores De Risco Em Saúde Sexual E Reprodutiva De Mulheres Presidiárias: Revisão Integrativa. Revista Baiana de Enfermagem. 2017;31.
14. Pinheiro W, Moreira D, Pedrosa H, Braga S, Sena A, Oliveira G, et al. Utilização do Protocolo de Registro Utstein durante as Manobras de Reanimação Cardiopulmonar: Revisão Integrativa / Use of the Utstein Protocol Record during the Cardiopulmonary Resuscitation Maneuver: Integrative Review. ID on line REVISTA DE PSICOLOGIA. 2020;14:478-886.
15. Soares CB, Hoga LAK, Peduzzi M, Sangaleti C, Yonekura T, Silva DRAD. Integrative Review: Concepts And Methods Used In Nursing. Revista da Escola de Enfermagem da USP. 2014;48:335-45.
16. Martins, J. D. N.,Sardinha, D. M.,Silva, R. R.,Lima, K. V. B.&Lima, L. N. G. C. (2020) As implicações da COVID-19 no sistema cardiovascular: prognóstico e intercorrências. J Health Biol Sci.
17. Bangalore S, Sharma A, Slotwiner A, Yatskar L, Harari R, Shah B, et al. ST-Segment Elevation in Patients with Covid-19 - A Case Series. N Engl J Med. 3822020. p. 2478-80.
18. Bardají A, Carrasquer A, Sánchez-Giménez R, Lal-Trehan N, Del-Moral-Ronda V, Peiró, et al. Prognostic implications of myocardial injury in patients with and without COVID-19 infection treated in a university hospital. Rev Esp Cardiol (Engl Ed). 2021;74(1):24-32.
19. Bavishi C, Bonow RO, Trivedi V, Abbott JD, Messerli FH, Bhatt DL. Special Article - Acute myocardial injury in patients hospitalized with COVID-19 infection: A review. Prog Cardiovasc Dis. 2020;63(5):682-9.
20. Bursi F, Santangelo G, Sansalone D, Valli F, Vella AM, Toriello F, et al. Prognostic utility of quantitative offline 2D-echocardiography in hospitalized patients with COVID-19 disease. Echocardiography. 2020;37(12):2029-39.
21. Cantador E, Núñez A, Sobrino P, Espejo V, Fabia L, Vela L, et al. Incidence and consequences of systemic arterial thrombotic events in COVID-19 patients. J Thromb Thrombolysis. 2020;50(3):543-7.
22. Cao L, Zhang S, Luo X, Wang E, Bai Y, Li Z, et al. Myocardium injury biomarkers predict prognosis of critically ill coronavirus disease 2019 (COVID-19) patients. Ann Palliat Med. 2020;9(6):4156-65.
23. Chen C, Li H, Hang W, Wang DW. Cardiac injuries in coronavirus disease 2019 (COVID-19). J Mol Cell Cardiol. 2020;145:25-9.
24. Chinitz JS, Goyal R, Harding M, Veseli G, Gruberg L, Jadonath R, et al. Bradyarrhythmias in patients with COVID-19: Marker of poor prognosis? Pacing Clin Electrophysiol. 2020;43(10):1199-204.
25. Efros O, Barda N, Meisel E, Leibowitz A, Fardman A, Rahav G, et al. Myocardial injury in hospitalized patients with COVID-19 infection-Risk factors and outcomes. PLoS One. 2021;16(2):e0247800-e.
26. Elias P, Poterucha TJ, Jain SS, Sayer G, Raikhelkar J, Fried J, et al. The Prognostic Value of Electrocardiogram at Presentation to Emergency Department in Patients With COVID-19. Mayo Clin Proc. 2020;95(10):2099-109.
27. Fredrich VCR, Nasr AMLF, Champion L, Mello TPdC, Silva JVAd, Ziak ML, et al. Perfil de óbitos por Covid-19 no Estado do Paraná no início da pandemia: estudo transversal. Rev Saúde Pública Paraná (Online). 2020;3(supl. 1):62-74.
28. Golpe R, Pérez-de-Llano LA, Dacal D, Guerrero-Sande H, Pombo-Vide B, Ventura-Valcárcel P. Risk of severe COVID-19 in hypertensive patients treated with renin-angiotensin-aldosterone system inhibitors. Med Clin (Barc). 2020;155(11):488-90.
29. Guerrero Pérez E, Andreu Cayuelas JM, Navarro Peñalver M,

Mateo Martínez A. Elevated baseline renin levels as a possible cause of worse prognosis of COVID-19 in patients with heart disease. Rev Esp Cardiol (Engl Ed). 2021;74(2):203-4.
30. Hamadeh A, Aldujeli A, Briedis K, Tecson KM, Sanz-Sánchez J, Al Dujeili M, et al. Characteristics and Outcomes in Patients Presenting With COVID-19 and ST-Segment Elevation Myocardial Infarction. Am J Cardiol. 2020;131:1-6.
31. Khan A, Althunayyan S, Alsofayan Y, Alotaibi R, Mubarak A, Arafat M, et al. Risk factors associated with worse outcomes in COVID-19: a retrospective study in Saudi Arabia. East Mediterr Health J. 2020;26(11):1371-80.
32. Li J, Xu G, Yu H, Peng X, Luo Y, Cao C. Clinical Characteristics and Outcomes of 74 Patients With Severe or Critical COVID-19. Am J Med Sci. 2020;360(3):229-35.
33. López-Otero D, López-Pais J, Antúnez-Muiños PJ, Cacho-Antonio C, González-Ferrero T, González-Juanatey JR. Association between myocardial injury and prognosis of COVID-19 hospitalized patients, with or without heart disease. CARDIOVID registry. Rev Esp Cardiol (Engl Ed). 2021;74(1):105-8.
34. Ma X, Wang H, Huang J, Geng Y, Jiang S, Zhou Q, et al. A nomogramic model based on clinical and laboratory parameters at admission for predicting the survival of COVID-19 patients. BMC Infect Dis. 2020;20(1):899.
35. Mengozzi A, Georgiopoulos G, Falcone M, Tiseo G, Pugliese NR, Dimopoulos MA, et al. The relationship between cardiac injury, inflammation and coagulation in predicting COVID-19 outcome. Sci Rep. 2021;11(1):6515-.
36. Pardo Sanz A, Salido Tahoces L, Ortega Pérez R, González Ferrer E, Sánchez Recalde Á, Zamorano Gómez JL. New-onset atrial fibrillation during COVID-19 infection predicts poor prognosis. Cardiol J. 2021;28(1):34-40.
37. Qin J-J, Cheng X, Zhou F, Lei F, Akolkar G, Cai J, et al. Redefining Cardiac Biomarkers in Predicting Mortality of Inpatients With COVID-19. Hypertension. 2020;76(4):1104-12.
38. Raad M, Dabbagh M, Gorgis S, Yan J, Chehab O, Dagher C, et al. Cardiac Injury Patterns and Inpatient Outcomes Among Patients Admitted With COVID-19. Am J Cardiol. 2020;133:154-61.
39. Rey JR, Caro-Codón J, Rosillo SO, Iniesta Á M, Castrejón-Castrejón S, Marco-Clement I, et al. Heart failure in COVID-19 patients: prevalence, incidence and prognostic implications. Eur J Heart Fail. 2020;22(12):2205-15.
40. Shang W, Dong J, Ren Y, Tian M, Li W, Hu J, et al. The value of clinical parameters in predicting the severity of COVID-19. J Med Virol. 2020;92(10):2188-92.
41. Si D, Du B, Ni L, Yang B, Sun H, Jiang N, et al. Death, discharge and arrhythmias among patients with COVID-19 and cardiac injury. Cmaj. 2020;192(28):E791-e8.
42. Xu H, Hou K, Xu R, Li Z, Fu H, Wen L, et al. Clinical Characteristics and Risk Factors of Cardiac Involvement in COVID-19. J Am Heart Assoc. 2020;9(18):e016807.