Cardiac Complications in Patients with COVID-19: An Integrative Literature Review

ABSTRACT

Objective: To verify, based on the literature, what the main cardiac complications are in patients with COVID-19, during treatment in a hospital unit. Materials and methods: An integrative review, carried out by searching for studies in eight national and international databases. The final sample consisted of 16 studies published between January and May 2020, which were subjected to structural evaluation by the following instruments: Case Report Guidelines, for case reports; and Strengthening the Reporting of Observational Studies in Epidemiology, for observational studies. Results: The main cardiac complications were predominantly obstructive events, herein understood as acute myocardial infarction, followed by severe arrhythmic conditions and heart failure, all due to the hyperinflammation condition resulting from viral infection. Conclusions: The knowledge about cardiac complications during COVID-19 treatment has become important, since it can collaborate for the adoption of more effective treatment protocols and guide the assistance offered by health professionals, in order to identify such complications and intervene early.

KEYWORDS (Source: DeCS)

Coronavirus infections; hospital care; cardiology; critical care; nursing care.

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Complicaciones cardíacas en pacientes con covid-19: revisión integrativa de la literatura

RESUMEN

Objetivo: verificar a partir de la literatura cuáles son las principales complicaciones cardíacas en pacientes con covid-19, durante el tratamiento en una unidad hospitalaria. Materiales y método: revisión integradora, realizada mediante la búsqueda de estudios en ocho bases de datos nacionales e internacionales. La muestra final estuvo conformada por 16 estudios publicados entre enero y mayo de 2020, que fueron sometidos a evaluación estructural, utilizando las Case Report Guidelines, para los reportes de caso, y el Strengthening the Reporting of Observational Studies in Epidemiology, para los estudios observacionales. Resultados: las principales complicaciones cardíacas fueron principalmente eventos obstructivos, entendidos aquí por infarto agudo de miocardio, seguidos de arritmias severas e insuficiencia cardíaca, todo debido a la condición de hiperinflamación por infección viral. Conclusiones: el conocimiento sobre las complicaciones cardíacas durante el tratamiento de la covid-19 ha cobrado importancia, ya que puede colaborar para la adopción de protocolos de tratamiento más efectivos y orientar la asistencia brindada por los profesionales de la salud, con el fin de identificar dichas complicaciones e intervenir tempranamente.

PALABRAS CLAVE (Fuente: DeCS)

Infecciones por coronavirus; atención hospitalaria; cardiología; cuidados críticos; atención de enfermería.
Complicações cardíacas em pacientes com covid-19: revisão integrativa da literatura

RESUMO

Objetivo: verificar, a partir da literatura, quais as principais complicações cardíacas em pacientes com covid-19, durante o tratamento em unidade hospitalar. Materiais e método: revisão integrativa, realizada mediante busca de estudos em oito bases de dados nacionais e internacionais. A amostra final foi constituída por 16 estudos publicados entre janeiro e maio de 2020, os quais foram submetidos à avaliação estrutural pelos instrumentos Case Report Guidelines, para os relatos de caso, e Strengthening the Reporting of Observational Studies in Epidemiology, para os estudos observacionais. Resultados: as principais complicações cardíacas foram predominantemente os eventos obstrutivos, entendidos aqui com infarto agudo do miocárdio, seguido dos quadros arrítmicos graves e da insuficiência cardíaca, todos devido ao quadro de hiperinflamação em decorrência da infecção viral. Conclusões: o conhecimento sobre as complicações cardíacas durante o tratamento da covid-19 tornou-se importante, visto que pode colaborar para a adoção de protocolos de tratamento mais eficazes e orientar a assistência ofertada pelos profissionais de saúde, a fim de identificar tais complicações e intervir precocemente.

PALAVRAS-CHAVE (FONTE: DECIS)

- Infecções por coronavírus;
- Assistência hospitalar;
- Cardiologia;
- Cuidados críticos;
- Cuidados de enfermagem.
Introduction

In 2019, more precisely in December, the first cases of the disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-CoV-2), a new category of coronavirus (1), were disclosed. The first cases occurred in the city of Wuhan, Hubei province, China, and, in less than 30 days, cases were reported in other countries and even on other continents (2).

Some authors described that it was a zoonosis, coming from wild animals, more precisely bats, with high pathogenicity in humans, affecting the airways first, causing severe acute respiratory syndrome and, subsequently, affecting other systems (3).

The viral disease, called "COVID-19", has an important potential for transmissibility via air and contact. It is a viral pneumonia, which affects the upper and lower airways, causing severe respiratory failure, with the need, in cases of too much effort by the individual, to offer oxygen by positive pressure, through mechanical invasive ventilation, that is, the patient will need uninterrupted care in an intensive care unit. In some cases, the disease causes progressive and rapid deterioration, leading to death (2).

In late January 2020, the World Health Organization declared that Sars-CoV-2, or COVID-19, became a public health emergency, that is, a pandemic (4, 5). Currently, COVID-19 has already affected the population of several countries in different continents, with contamination records higher than those of other diseases transmitted by air, such as, for example, influenza, and high mortality in older adults and in individuals with pre-existing chronic diseases (6-8).

Due to the emergency, several therapeutic approaches have been adopted and successful ones have been disseminated in several countries. Studies were carried out that sought to approve the efficacy of drugs such as hydroxychloroquine®, alpha-interferon® and lopinavir®; however, they were non-randomized and unblinded studies, which negatively interfered with the level of evidence of the publications. There were also some adverse cardiovascular effects, such as, for example, prolongation of the QT interval, arrhythmias and an increased risk of sudden death (9-11), based on the drug interaction between some drugs of different pharmacological groups.

Respiratory repercussions —fever, cough, pharyngitis, fatigue and complications related to pneumonia and respiratory syndrome—are the first symptoms in individuals considered symptomatic. However, a number of studies have revealed the involvement of other systems, such as the cardiac one, from the onset of tachyarrhythmias and signs of cardiac failure (12, 13). In other Chinese studies, in addition to the complications described above, ischemic cardiac events, characteristic of acute myocardial infarction in patients with COVID-19 (14-16), were identified.

Obstructive conditions in individuals with previous coronary artery disease (CAD) and other conduction or mechanical disorders have contributed to the worsening of patients who require intensive care. Some authors highlight the presence of comorbidities, such as systemic arterial hypertension (SAH) and/or diabetes mellitus (DM), as risk factors for the development of cardiac complications during care for individuals with COVID-19. The treatment of these chronic diseases with angiotensin-converting enzyme inhibitors and angiotensin-2 receptor blockers increases the bioavailability of the angiotensin-converting enzyme 2, which is the target molecule of Sars-CoV-2, found in the epithelial pulmonary, intestinal, and renal tissues, as well as in blood vessels (17, 18).

As it is an emerging disease with a varied pathogenic profile that triggers important systemic repercussions in order to favor the involvement of the heart, it was sought to identify, based on the literature, what the main cardiac complications are in patients with COVID-19 during hospital treatment.

Materials and methods

This is an integrative review, based on articles published from January to May 2020. The phases related to the study method were distributed sequentially: a) identification of the research question; b) establishment of criteria for the inclusion and exclusion of studies found in the literature; c) definition of the information to be extracted from the selected studies in line with the guiding question; d) evaluation of the studies included in the review; e) interpretation of the results found; and f) synthesis of knowledge (19-21).

The selection phase of the studies took place in the first half of June 2020, by means of an electronic search paired with original articles and case reports, given the pandemic nature of the disease, which answered the research question, by using the Pico (22) (acronym for patient, intervention, control or comparison and outcomes) strategy, according to Table 1, to construct the
following question: Is there scientific evidence in the literature about the main cardiac complications in patients with COVID-19 during hospital treatment?

The final sample consisted of articles published in full, from primary studies or case reports in which the main cardiac complications were evident; published in 2020, in Portuguese, English or Spanish. Articles that did not describe the main cardiac complications during the hospitalization period of patients with COVID-19 were excluded.

The electronic databases accessed were Medical Literature Analysis and Retrieval System Online (Medline), via PubMed; Scopus, via Elsevier; Cumulative Index to Nursing and Allied Health Literature (Cinahl), via EBSCO; Latin American and Caribbean Literature on Health Sciences (Literatura Latino-americana e do Caribe em Ciências da Saúde, Lilacs); Spanish Bibliographic Index on Health Sciences (Índice Bibliográfico Español en Ciencias de la Salud, IB ECS), Nursing Database (Base de Dados de Enfermagem, BDEnf), via the Virtual Health Library; Web of Science; and Embase. The choice of these databases was justified by the emerging characteristic of the investigated disease, which allowed for the use of controlled and uncontrolled descriptors (keywords) in a combined manner, using the Boolean operators AND and OR, as described in Table 2.

### Table 1. Description of the research question with the use of the PICO strategy. Ribeirão Preto, São Paulo, Brazil, 2020

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
<th>Description</th>
<th>Practical question component</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Intervention</td>
<td>Treatment of patients with COVID-19 in hospital units.</td>
<td>Treatment in non-critical unit or in critical unit (Intensive Care Unit)</td>
</tr>
<tr>
<td>C</td>
<td>Comparison</td>
<td>Does not apply.</td>
<td>Does not apply.</td>
</tr>
<tr>
<td>O</td>
<td>Outcome</td>
<td>Cardiac repercussions during the treatment for COVID-19.</td>
<td>Main cardiac complications during the treatment for COVID-19.</td>
</tr>
</tbody>
</table>

Source: Elaborated by the authors based on research data.

### Table 2. Combinations searched in the databases: Medline, Scopus, Cinahl, Lilacs, IB ECS, BDEnf, Web of Science and Embase. Ribeirão Preto, São Paulo, Brazil, 2020

<table>
<thead>
<tr>
<th>Databases</th>
<th>Combinations in the aforementioned databases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medline/PubMed MeSH</td>
<td>(&quot;coronavirus&quot;) AND (&quot;Cardiovascular disease&quot;)</td>
</tr>
<tr>
<td>Scopus Keywords</td>
<td>(&quot;covid-19&quot;) AND (&quot;complications&quot;) AND (&quot;cardiac&quot;)</td>
</tr>
<tr>
<td>Cinahl Titles</td>
<td>(&quot;coronavirus infection&quot;) AND (&quot;cardiac patients&quot;) OR (&quot;coronavirus infection&quot;) AND (&quot;cardiac output, decreased&quot;)</td>
</tr>
<tr>
<td>Lilacs DeCS descriptors</td>
<td>(&quot;coronavirus infection&quot;) AND (&quot;cardiovascular disease&quot;)</td>
</tr>
<tr>
<td>Web of Science Keyword</td>
<td>(&quot;covid-19&quot;) AND (&quot;complications&quot;) AND (&quot;cardiac&quot;)</td>
</tr>
<tr>
<td>Embase Entree</td>
<td>(&quot;coronavirus infection&quot;) AND (&quot;cardiovascular disease&quot;)</td>
</tr>
<tr>
<td>IB ECS DeCS descriptors</td>
<td>(&quot;infecciones por coronavirus&quot;) AND (&quot;enfermedades cardiovasculares&quot;) OR (&quot;infecciones por coronavirus&quot;) AND (&quot;doenças cardiovasculares&quot;)</td>
</tr>
<tr>
<td>BDEnf DeCS descriptors</td>
<td>(&quot;infeções por coronavirus&quot;) AND (&quot;doenças cardiovasculares&quot;)</td>
</tr>
</tbody>
</table>

Source: Elaborated by the authors based on research data.
The option to use controlled descriptors, in the Medline/PubMed, Cinahl, Lilacs, Embase, IBECS and BDEnf databases, and uncontrolled descriptors, in Scopus and Web of Science, occurred because the search was supported in eight databases, with the objective of integrating information about the theme under study.

The combinations and data analysis were carried out independently by the researchers, respecting the inclusion and exclusion criteria described above. Then, the reading of the titles was conducted and those that described the cardiac complications were selected. After this process, the articles were inserted in the Mendeley (20) reference manager to separate duplicate studies.

After the analysis of the titles, careful readings of the abstracts were carried out and those that approached the central subject matter, proposed by the guiding question, were selected for full-reading. For consolidation, reading and evaluation were performed, and 16 articles were included in the final sample, which showed cardiac complications through the clinical evolution of the investigated patients, results of laboratory tests, and imaging that showed worsening of the clinical condition.

From the selection of articles, the structural consistency was evaluated, using the following instruments: Case Report Guidelines (Care), for case reports, and Strengthening the Reporting of Observational Studies in Epidemiology (Strobe), for observational studies. Such instruments represent international guidelines for the construction of research reports (23-25).

Care consists of 13 topics: title, keywords, abstract, introduction, information about the patient, clinical aspects, history, diagnosis, treatment/interventions, outcome, discussion, perspective, and patient consent (24). On the other hand, Strobe consists of 22 items: title and abstract; introduction, which includes the justification and objectives; method, which shows the type of study, location, participants, variables, quantitative variables, bias, data collection, data analysis and statistical analysis; results, which bring the number of participants, characterization of the participants, main results, outcome, and other analyses; discussions, which contemplate the key results, limitations, interpretation and generalization; finally, other information with emphasis on the funding of the study, if any (24).

Due to the fact that the review proposal is related to an emerging disease and little described in the literature until then, it was sought to highlight the structural consistency of each study from the analysis, using the Care and Strobe instruments. All the selected studies covered the description of all items concerning each type of study. The methodological quality assessment of the selected studies was performed by the authors based on the Critical Appraisal Checklist for Systematic Review and Research Synthesis tool of the Joanna Briggs Institute (25-27).

The extraction of information related to the main cardiac complications occurred after the consolidation of the final sample of articles included in the present review, with information extracted for the characterization of the manuscript (name of the authors, database, year, title and journal) and the presentation itself of the methodological design, the study population, and the main cardiac complications found.

**Results**

For the description of the search process, the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow diagram was used in order to guide the selection of studies (26), as shown in Figure 1.

A total of 49 articles were selected for reading their titles; of these, 14 were excluded because they were not primary studies or case reports, leaving 35 articles for reading their abstracts, with the exclusion of 19 articles for not describing cardiac complications in patients with COVID-19 during hospital treatment.

After a careful selection, 16 studies made up the final sample of articles, seven of which were published in journals indexed in Scopus, one in Web of Science, one in Embase and seven in Medline, all published in 2020 and in English. The other databases searched did not have studies selected to compose this review.

The selected studies were published in electronic and publicly accessible journals, with seven being published in journals in the cardiovascular area and the others in journals in other areas.

As for the type of study, 14 were observational studies (cohort or cross-sectional) and three were case reports. The sample consisted of 14 studies developed in China, two in Italy, and one in England. Regarding the objectives, four were related to cardiac complications of patients with COVID-19, seven to cardiovascular complications, naming cardiac complications, and the others referred to complications in general, with emphasis on adverse cardiac events during treatment.
emerging disease, with a pathogenic potential to be known and therapeutics still being implemented in several countries. Despite the limitations described, the present study advances from the summary of the results regarding care for patients with COVID-19 during hospitalization.

According to Table 3, the cardiac complications described by the authors of the selected articles were arrhythmias (1, 2, 15, 28, 31, 32), changes in the conduction of the electrical impulse generated by the physiological pacemaker of the heart; acute heart injury (1, 7, 8, 12, 17, 32), myocardial injury (2), coronary heart disease (14, 31-34), obstructive coronary disease (15, 16, 28, 30, 31) and heart failure (15, 28, 32).

Seeking to conceptually understand the complications highlighted by the authors of the selected studies, it was verified that the expressions “acute cardiac injury”, “myocardial injury”, “coronary heart disease” and “obstructive coronary disease” are synonymous, as they were acute diseases centered on the obstruction of the coronary arteries, identified from the laboratory findings (elevation of troponin I, myoglobin creatinophosphokinase [CKMB] and creatine kinase [CK]) and the description of signs and symptoms presented by the participants of the studies that composed this review.

Within the sample of selected articles, those that showed the main cardiac complications in hospitalized patients with COVID-19 were included, even considering studies with participants with pre-existing diseases, such as cardiovascular diseases (CVDs), as they tend to increase the risk of developing more severe conditions in patients with COVID-19, mainly due to the onset of obstructive events and the presence of a systemic inflammatory response (35, 36).

All the selected studies (1, 2, 8, 13-17, 28-34) for the final sample of this review brought coronary obstructive events as the main cardiac complication evidenced during hospitalization of patients with COVID-19. The obstructive events predominantly represented by acute myocardial infarction are possibly the result of an increased myocardial workload during infections, which cause myocardial injuries (37, 38-40). In addition, Sars-CoV-2 has been shown to trigger an exaggerated systemic inflammatory response, which, in addition to acute lung injury and acute respiratory distress syndrome, can lead to multiple cardiovascular complications (32, 34), unstable angina, tachycardia, heart failure, stroke, cardiogenic shock and even cardiopulmonary arrest (37, 39).
### Table 3. Studies selected to compose the review, according to authors, database, title, journal, methodological design, and cardiac complications. Ribeirão Preto, São Paulo, Brazil

<table>
<thead>
<tr>
<th>Authors and database</th>
<th>Title and journal</th>
<th>Methodological design</th>
<th>Population</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lei et al. (1) Scopus</td>
<td>Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. <em>E Clinical Medicine</em></td>
<td>Cross-sectional and retrospective study.</td>
<td>34 Chinese patients submitted to surgery.</td>
<td>Arrhythmia and acute cardiac injury.</td>
</tr>
</tbody>
</table>
Patients hospitalized with COVID-19 tend to have high serum levels of CK and lactate dehydrogenase. Evidence of myocardial injury, such as increased levels of high cardiac troponin I (cTnI) (> 28 pg/mL), can contribute to the emergence of obstructive events throughout treatment (41). Elevation of biomarkers (troponin I and CKMB), as well as electrocardiographic and echocardiographic changes were observed, revealing a condition of coronary obstruction during hospitalization (38, 39).

Obstructive injury is caused by the rupture of the plaque or thrombus in the vessel walls, by the proliferation of cytokines, by the reduction of oxygen in the heart muscle, by coronary spasm, by microthrombi or by direct endothelial or vascular injury (7, 8, 12, 17, 32, 33, 34, 38, 42, 43). Such situations described lead to an obstructive condition, reflected by changes in the cardiac biomarkers and electrocardiographic changes, especially the elevation of the ST segment.

Most of the studies revealed the relationship between laboratory and imaging findings by electrocardiographic examination in patients with comorbidities (38, 44, 45). The increase in troponin I and CKMB, combined with depression of the ST segment and/or inverted T wave at electrocardiographic examination, increased the risk of death, when combined with systemic arterial hypertension in patients with DM (17, 29).

The progressive increase in the biomarkers, in addition to indicating coronary obstructive events, can signal the development of systemic complications, such as disseminated intravascular coagulation (45, 46). This finding considerably raises the mortality rates due to COVID-19 (8, 12), especially in patients with a previous history of SAH, DM, dyslipidemia and/or CAD (16, 33, 34, 38). From this perspective, it can be said that CVDs are considered important risk factors for the occurrence of cardiac complications during hospitalization, increasing the potential for severity and deaths, especially in aged patients (15, 29, 30, 31, 32, 33, 38).

In this perspective, the importance of monitoring cardiac biomarkers throughout hospitalization was perceived in order to anticipate cardiac complications, especially in patients with COVID-19 who have previous comorbidities.

Arrhythmias were highlighted in six (1, 2, 15, 28, 31, 32) of the 16 articles included in the final sample of this review; however, only one (15) of them highlighted heart rate. Atrial fibrillation was highlighted as the most common cardiac complication, due to changes in the electrocardiographic tracing, in addition to increased serum levels of hypersensitive cTnI, in patients with COVID-19 admitted to intensive care units (15). In the other articles (1, 2, 28, 31, 32), the electrocardiographic changes which occurred during hospitalizations of patients with COVID-19 were not described; however, the authors pointed out that arrhythmic conditions can increase the severity of the COVID-19 patients' clinical conditions, due to the presentation of severe cardiac rhythms that evolve to cardiopulmonary arrest, especially in patients with cardiovascular comorbidities identified on admission to the hospital unit.

The Centers for Disease Control and Prevention conducted a survey with 72 patients admitted to a North American medical center, of whom 43 had CVDs, six presented cardiac complications, such as supraventricular tachycardia, atrial fibrillation, atrial flutter or complete atrial ventricular block (35). Thus, it was perceived that the arrhythmic conditions need to be identified early so that therapeutic approaches can be taken, with the aim of restoring sinus rhythm.
Heart failure was evidenced in three of the 16 studies included in the final sample of this review. All the articles were developed with adult and aged patients diagnosed with COVID-19, with pre-existing CVDs; however, the development of heart failure was predominantly related to the advanced age profile of the patients under study (15, 28, 32). It was also verified that the left ventricular ejection fraction of less than 40\%, at echocardiographic examination in cases of heart failure, combined with elevated serum troponin I and elevated ST segment at electrocardiographic examination, favor the worsening of COVID-19 patients’ prognoses (36, 38-40).

Infection with Sars-CoV-2 is a mild disease in most people, although a small portion of patients affected by the virus has developed severe respiratory failure characterized by a hyperinflammatory syndrome. Dysfunction of the vascular endothelial cell promoted by viral infection, combined with myocardial depression associated with inflammation, stress cardiomyopathy and/or the host’s response can cause or worsen heart failure, demand-related ischemia and arrhythmias (32).

Many discussions have occurred about cardiac complications, diagnosed based on the existence of the arrhythmic conditions identified through electrocardiographic tracings and obstructive events in coronary arteries, verified by electrocardiographic and echocardiographic changes, and by the measurement of cardiac biomarkers (47-49). From the synthesis of the findings in the texts, it was perceived that cardiac complications can occur at different periods of hospitalization (40-52) and that the presence of comorbidities (38, 49) can promote worsening of the clinical condition of patients with COVID-19.

In summary, the studies that comprised this review allowed highlighting the importance of the cardiac monitoring of patients undergoing COVID-19 treatment, with the aim of intervening early in the reversal of arrhythmic conditions and verifying electrocardiographic findings corresponding to obstructive myocardial injury and heart failure. Some studies highlighted the importance of monitoring cardiac biomarkers in order to make increasingly anticipate the therapeutic approaches.

The study limitation was the number of articles on the subject matter that accurately revealed cardiac complications in patients with COVID-19 during hospitalization, through primary studies and with methodological consistency. Until June 2020, there are many studies underway that will allow greater knowledge about the disease and its complications.

**Conclusions**

The cardiac complications that most emerged were coronary obstructive events, arrhythmic conditions, and heart failure. It was perceived that such complications can be related to the previous existence of CVDs, verified on admission to the hospital unit, predominantly in patients over the age of 60, who have contracted COVID-19.

Knowledge about cardiac complications during the treatment of patients with COVID-19 has begun to emerge, since it can contribute to the adoption of more efficient care protocols in order to prevent such complications, which leads to favorable outcomes, mainly related to patients with CVDs.

**Conflict of interest:** None declared.
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