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Pandemic COVID-19 and its relationship with cardiovascular disease: integrative review

Pandemia COVID-19 y su relación con enfermedad cardiovascular: revisión integrativa Pandemia COVID-19 e sua relação com a doença cardiovascular: revisão integrativa

ABSTRACT

Objective: To identify current scientific evidence in the literature on the relationship between COVID-19 and cardiovascular diseases. Methods: This is an integrative literature review, carried out in the databases: PubMed, Chocrane, EBSCO, Scopus database, Science of Direct virtual library and LILACS. The inclusion criteria were studies made available in their entirety from April to June 2020 and that answered the guiding question: What has the literature pointed out about the manifestations of the Covid-19 pandemic in patients with cardiovascular diseases? Results: Six articles were included; that allowed to explore the current evidence on cardiovascular diseases and the pandemic by covid-19. Results showed recommendations and proposals for the care of these patients. Conclusion: Studies have pointed out relevant impacts caused by infection with the new coronavirus and the cardiovascular system, highlighting the need for new research that encompasses the theme, as it still represents a wide challenge for the management of infected patients.

DESCRIPTORS: Coronavirus Infections; Pandemics; Cardiovascular Disease; Prevention and Control; Health System.

RESUMEN

Objetivo: Identificar la evidencia científica actual en la literatura sobre la relación entre COVID-19 y enfermedades cardiovasculares. Métodos: Se trata de una revisión integradora de la literatura, realizada en las bases de datos: PubMed, Chocrane, EBSCO, base de datos Scopus, biblioteca virtual Science of Direct y LILACS. Los criterios de inclusión fueron estudios que se pusieron a disposición en su totalidad de abril a junio de 2020 y que respondieron a la pregunta orientadora: ¿Qué ha señalado la literatura sobre las manifestaciones de la pandemia Covid-19 en pacientes con enfermedades cardiovasculares? Resultados: Se incluyeron seis artículos; que permitió explorar la evidencia actual sobre enfermedades cardiovasculares y la pandemia por covid-19. Los resultados arrojaron recomendaciones y propuestas para el cuidado de estos pacientes. Conclusión: Los estudios han señalado impactos relevantes provocados por la infección por el nuevo coronavirus y el sistema cardiovascular, destacando la necesidad de nuevas investigaciones que abarquen la temática, ya que aún representa un gran desafío para el manejo de los pacientes infectados.

DESCRIPTORES: Infecciones por Coronavirus; Pandemias; Enfermedades Cardiovasculares; Prevención y Control; Sistemas de Salud.

RESUMO

Objetivo: Identificar na literatura evidências científicas atuais sobre a relação entre COVID-19 e doenças cardiovasculares. Métodos: Trata-se de uma revisão integrativa da literatura, realizada nas bases de dados: PubMed, Chocrane, EBSCO, Banco de dados Scopus, Biblioteca virtual Science of Direct e LILACS. Os critérios de inclusão foram estudos disponibilizados na integra no período de abril a junho de 2020 e que respondesse à questão norteadora: O que a literatura tem apontado sobre a as manifestações da pandemia por Covid-19 em portadores de doenças cardiovasculares?. Resultados: Foram incluídos seis artigos; que permitiram explorar as evidências atuais sobre as doenças cardiovasculares e a pandemia pelo covid-19. Resultados evidenciaram recomendações e propostas para atendimento destes pacientes. Conclusão: Estudos apontaram impactos relevantes provocados pela infecção pelo novo coronavírus e o sistema cardiovascular, ressaltando a necessidade de novas pesquisas que englobem a temática, pois ainda representa um amplo desafio para o manejo dos pacientes infectados.

DESCRITORES: Infecções por Coronavírus; Pandemias; Doenças Cardiovasculares; Prevenção e Controle; Sistemas de Saúde

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Bárbara Caroliny Pereira Costa

Nurse. University of São Paulo, Ribeirão Preto School of Nursing, Ribeirão Preto, SP, Brazil. ORCID: 0000-0003-3945-5240

Mayara Rocha Siqueira Sudré

Nurse. University of São Paulo, Ribeirão Preto School of Nursing, Ribeirão Preto, SP, Brazil. ORCID: 0000-0002-9515-5907

Isabela Gomes Musa dos Santos

Nurse. Women's Beneficent Society Sírio-Libanês Hospital, São Paulo, SP, Brazil. ORCID: 0000-0002-6174-0155

Damiana Rodrigues

Nurse. IFSULDEMINAS-Passos, Passos, MG, Brazil. ORCID: 0000-0002-2405-1860

Juliana Pereira Machado

Nurse. Barão de Mauá University Center. Ribeirão Preto, SP, Brazil. ORCID: 0000-0003-2225-8355

Eugenia Velludo Veiga

Nurse. University of São Paulo, Ribeirão Preto School of Nursing, Ribeirão Preto, SP, Brazil. ORCID: 0000-0003-3677-0210

INTRODUCTION

urrently, the world has experienced a pandemic unprecedented in history, related to the infection caused by the new coranavirus. Among the main complications, we highlight the severe acute respiratory diseases, the syndrome called SARS-CoV-2 or COVID-19, with mention of the year of appearance, at the end of 2019, in Wuhan, Hubei province, China. (1-2)

Coronavirus is transmitted by inhalation or contact with infected droplets and its incubation period varies between 2 and 14 days. Many people can be asymptomatic, and the case mortality rate is estimated to range from 2 to 3%. (3-4)

According to data from the World Health Organization (WHO), 7.368.114 cases of COVID-19 and 416.536 deaths have been confirmed worldwide (as of June 10, 2020). As of this date, Brazil already had 742.084 confirmed cases and 38.497 deaths by COVID-19. (5)

Treatment is essentially supportive, with domestic isolation for cases with mild disease development. Prevention involves quarantine and surveillance of suspected cases, social detachment, hand hygiene and the use of masks in public places. The virus spreads more rapidly than SARS-COV and the Middle Eastern coronavirus

(MERS-CoV), and has shown a lower fatality rate in developed countries. (5)

The symptoms usually presented are fever, cough, sore throat, dyspnea, fatigue, malaise among others. Its manifestation is mild in most people, however in people with comorbidities it can progress to pneumonia, acute respiratory distress syndrome (ARDS) and multiple organ dysfunction. ⁽⁶⁾

The relationship between cardiovascular events such as myocardial infarction (AMI), related to the influenza virus and pneumococcal infections is already known. (7) However, in the current pandemic, attention is drawn to the cardiac complications that COVID-19 has caused. (8) The presence of myocarditis, cardiac arrest and acute heart failure in patients with COVID-19 suggests the existence of a close relationship between SARS-CoV-2 infection and heart disease. (9)

A report on 99 patients hospitalized for SARS-CoV-2-related pneumonia in January 2020 in Wuhan, China, showed preexisting cardiovascular disease-CVD in 40% of them. (10) Another study showed that patients with end-stage heart failure had higher rates of mortality and myocardial injuries associated with COVID-19. (11)

Cardiovascular risk factors and conditions related to CVD should be carefully studied, according to guidelines based on current scientific evidence. (12)

Study stresses that previous cardiovascular diseases risk having increased levels of Angiotensin 2 Converting Enzyme (ACE 2) which can occur in more serious manifestations related to COVID-19, as the SARS-Cov 2 virus has the SKIPE binding protein in its structure, which binds to ACE 2, which facilitates its entry, replication and deregulation in the host cell. (13)

In this context, the European Society of Cardiology (ESC), proposes guidelines for the conduct of covid-19. This document covers the management of cardiac patients facing infection by Sars-Cov-2, as it is capable of presenting as arterial or venous thrombosis in acute coronary syndrome or leading to thromboembolism, it can also cause myocarditis and be harmful to patients with cardiac insufficiency. In this context, the European Society of Cardiology (ESC), proposes guidelines for the conduct of covid-19. This document covers the management of cardiac patients facing infection by Sars-Cov-2, as it is capable of presenting as arterial or venous thrombosis in acute coronary syndrome or leading to thromboembolism, it can also cause myocarditis and be harmful to patients with cardiac insufficiency. (12)

Given the scenario of uncertainties regarding the impact of the pandemic on people's health, especially in patients with installed CVD or associated risk factors, it becomes a priority focus to understand what is the

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relationship between cardiovascular diseases and the manifestations of COVID-19 in these patients. Thus, the aim of the study was to identify current scientific evidence in the literature on the relationship between COVID-19 and CVD.

METHODS

Integrative review, with a synthesis of multiple published studies and general conclusions regarding a specific study area, aims to optimize time; provides evidence for practice by making current scientific content available, with critical analysis and synthesis of results from other research. This review fulfilled the stages of construction of the guiding question, sample composition, categorization of studies, analysis of included studies, interpretation of results and construction of the review. (14)

To elaborate the question of this review, the PICO strategy was used, represented by the acronym of the English terms "Patient/Problem", "Intervention", "Comparison" and "Outcomes". The strategy is applied in the initial phase in order to identify keywords for the location of relevant studies in the selected databases. (15)

In this study, P refers to the problem of Covid-19 and CVD; o I as Intervention or indicator, to the relationship between Covid-19 and CVD. The C, as Comparison or control, in this case does not apply, and the C as an outcome, to verify what the literature has pointed out about the manifestations of the pandemic by Covid-19 in patients with CVD. Guiding question of the study: What the literature has pointed out about the manifestations of the pandemic by Covid-19 in patients with cardiovascular diseases.

For the selection of articles, full articles were published, published from 2019 to 2020, in Portuguese, English or Spanish, with the central theme of the relationship between COVID-19 and CVD. Gray literature texts or whose theme was incompatible with the proposal of this study after reading were excluded.

The bibliographic search was carried out from April to June 2020 in the databases National Library of Medicine National

Institutes of Health (PuBMed), Latin American and Caribbean Literature in Health Sciences (LILACS), EBSCO, in the Database Scopus, the Cochrane Library and the Science of Direct virtual library.

In the screening phase of the articles, the screening program called Rayyan® was used, which allows the optimization of literature reviews. (16) The program shows the title, summary, date of publication of the texts uploaded from the databases for the researcher to analyze, with an option of inclusion or exclusion, in addition to a tab designated as "maybe", in case the researcher has doubts in the inclusion and want to review the appropriate article. In the end, the program allows an organization of the review, in which the researcher will know how many articles were excluded, included and duplicated.

Após a seleção dos artigos no Rayyan°, foi utilizada a estratégia PRISMA para promover o relato da presente revisão. A recomendação PRISMA consiste em um checklist com 27 itens e um fluxograma de quatro etapas com intuito de ajudar os autores a melhorarem o relato de revisões sistemáticas e meta-análises. (17) Figure 1 illustrates the steps in the selection process for the studies included in this review as recommended by the flow chart Preferred Reporting Items for Systematic Review and Meta-Analyses – PRISMA(18), adapted for this study.

To extract data from the articles included

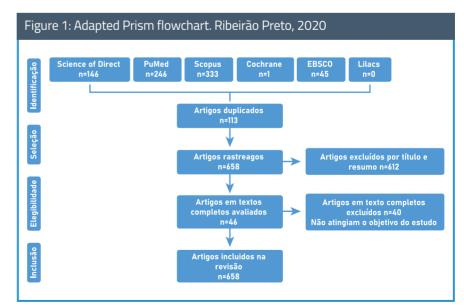
in the integrative review, an instrument was used that contemplates the following items: identification of the original article, methodological characteristics of the study, evaluation of methodological rigor, of the measured interventions and the results found. (19) The analysis of the data consisted of the exploration of the material after detailed readings of the articles, making cuts in record units.

The works included in the review were analyzed in Levels of Evidence (LE), which classifies the quality of the studies into seven levels: Level I (systematic reviews or meta--analysis of clinical study with randomization); Level II (clinical study with randomization); Level III (clinical study without randomization); Level IV (cohort study and case control); Level V (systematic review of descriptive/qualitative studies); Level VI (descriptive/qualitative studies); Level VII (expert opinion). According to this classification, levels I and II are considered strong evidence, levels III and IV are considered moderate evidence and levels V to VII are weak evidence. (20)

The data extracted from the studies were analyzed, interpreted and presented descriptively in a summary table.

RESULTS

In order to identify in the literature, what are the current scientific eviden-



ces about the relationship between CO-VID-19 and CVD, this review has a total of six studies, being 4 (66,66%) descriptive, 1 (16,66%) clinical trial and 1 (16,7%) retrospective observational.

Regarding the origin of the studies, the continents are distributed among North America, with 3 studies (50,0%), followed by the Asian, European and Oceania continents with 1 study each (16,7%). All were

published in the English language (100%) and a study with this theme has not been identified in Brazil so far.

Regarding the levels of evidence, 6 (100%) were classified as level VI (descriptive/qualitative studies), which gives a weak level of evidence. Table 2 summarizes the articles according to title, authors, year of publication, main objective, type of study and main results/conclusion.

DISCUSSION

This review identified in the literature, what is the current scientific evidence on the relationship between COVID-19 and CVD. Their results showed recommendations and proposals for the care of these patients.

Specifically on clinical complications, only one article evaluated the occurrence of

Chart 2 - Articles selected in the sample according to authors, year of publication, main objective, type of study and main results, 2020.				
TÍTULO	OBJETIVO	TIPO DE ESTUDO	RESULTADOS	
Artigo 1 Deng Q. et al(24). 2020. China	Verificar se a miocardite e a lesão miocárdica foram causadas pelo COVID-19.	Retrospectivo	Foram incluídos no estudo 112 pacientes com COVID-19. Houve evidências de lesão do miocárdio em pacientes com COVID-19; 14 (12,5%) dos pacientes apresentaram anormalidades semelhantes à miocardite. A maioria dos pacientes apresentou níveis normais de troponina na admissão, sendo que em 42 (37,5%) houve aumento de troponina durante a internação, principalmente nos que foram a óbito.	
Artigo 2 Khera A. et al(25). 2020. EUA	Destacar as ramificações da pandemia de COVID-19 para práticas de atendimento ambulatorial e modificação de fatores de risco em pacientes com alto risco de doença cardiovascular	Descritivo	Pacientes infectados com COVID-19 com pelo menos uma condição de saúde subjacente ou outro fator de risco tiveram resultados piores se comparados àqueles sem essas comorbidades. As condições preexistentes mais comuns em pacientes infectados foram diabetes mellitus (10,9%), doença pulmonar crônica (9,2%) e doença cardiovascular (9,0%). Sempre que possível, é fortemente recomendado continuar as visitas via telessaúde, e os pacientes devem ser aconselhados a relatar prontamente novos sintomas.	
Artigo 3 Mahmud E. et al(27). 2020. EUA	Fornecer recomendações para uma abordagem sistemática para o atendimento de pacientes com infarto agudo do miocárdio (IAM) durante a pandemia de COVID-19.	Descritivo	Os autores reconhecem como grande desafio fornecer recomendações para o tratamento da IAM na era COVID-19. As manifestações cardiovasculares de COVID-19 são complexas, com pacientes apresentando IAM, miocardite simulando IAM com supradesnivelamento do segmento ST, cardiomiopatia de estresse, cardiomiopatia não isquêmica, espasmo coronariano ou lesão miocárdica inespecífica, diante da prevalência de COVID-19 na população dos EUA ser desconhecida, com risco de disseminação assintomática.	
Artigo 4 Virani S.A. et al(28). 2020. Canadá	Fornecer perspectivas da liderança da Sociedade Canadense de Insufi- ciência Cardíaca (CHFS) sobre como otimizar o atendimento à IC duran- te a pandemia de COVID-19.	Descritivo	Dentre as soluções para desafios decorrentes da pandemia de COVID-19, o estudo propõe abordagens de cuidados remotos que possam ser aplicadas de maneira personalizada para otimizar o atendimento de pacientes com IC. Além disso, propõe a transição do atendimento tradicional para um sistema de atendimento virtual baseado em consultas por meio virtual ou de telessaúde, mantendo consultas presencias apenas aos pacientes mais graves.	

Artigo 5 Arnold. et al(29) 2020. Austrália	Apresentar um documento de con- senso de recomendações para a prestação de serviços cardíacos em áreas rurais e remotas durante a pandemia do COVID-19	Descritivo	O COVID-19 trouxe demandas significativas nos servi- ços cardiovasculares regionais e rurais da Austrália e da Nova Zelândia. Diante disto, algumas recomendações foram sugeridas para a prestação dos serviços cardio- vasculares, dentre elas o acesso aprimorado à consulta de telessaúde para pacientes ambulatoriais regionais e rurais, bem como a oferta de serviços de leitura eletro- cardiográfica (ECG) por especialista.
Artigo 6 Abdelazi. et al(30). 2020 Inglaterra	Examinar o impacto da pandemia de COVID-19 nas doenças relacio- nadas ao paciente, atraso no aten- dimento ao infarto do miocárdio com SST em um centro de atendi- mento terciário no Reino Unido.	Observacional retrospectivo	Dos 115 participantes do estudo, foram divididos em dois grupos, um grupo denominado "era COVID n = 46", e outro grupo denominado "era pré - COVID n = 69". Além disso, o estudo constatou também que durante o atual surto do COVID-19, médicos e organizações de saúde devem aumentar a conscientização do público de que a mensagem "Fique em casa" não deve ser mal interpretada de forma que as pessoas ignorem sintomas significativos de eventos como síndromes coronárias agudas, e incentivem as pessoas a procure aconselhamento médico em tempo hábil.

myocarditis due to COVID-19 in patients with CVD. Another study retrospectively assessed the impact of the pandemic on the treatment of AMI with supra.

In the development of this integrative review, the evidence generated provided support for assessing the relationship of COVID-19 in people with CVD. However, most of the articles analyzed presented levels of evidence considered weak, which indicates the need to develop studies with strong levels of evidence, capable of supporting safe and effective practices.

The studies analyzed have shown that people with CVD may be more susceptible to a higher mortality rate and that such patients require intensive care. Still, among the few studies on CVD and CO-VID-19 available, one points out that these patients can be considered a risk group for complications in the presence of SAR-S-COV-2 infection. (21)

The main clinical manifestation of CO-VID-19 is respiratory disease, with involvement of the cardiovascular system occurring less commonly, in approximately 8 to 12% of all patients. Systemic inflammation and thrombogenesis caused by the virus can affect the cardiovascular system with several manifestations such as myocardial injury, heart failure, Takotsubo's syndrome, arrhythmias, myocarditis and shock. The cardiac abnormality most commonly reported in

COVID-19 is defined as the significant increase in cardiac troponins. (11,21-22)

A study carried out in China points out that the cause of Covid-19 in a patient with CVD is the fact that SARS-CoV-2 infects host cells through the angiotensin-converting enzyme 2 and that this can cause damage to the myocardium, although it requires more studies to prove it. The angiotensin-converting enzyme 2 is a membrane-bound aminopeptidase that plays a vital role in the cardiovascular and immune systems. In addition, the angiotensin-converting enzyme 2 has been identified as a functional receptor for coronaviruses, including SARS-CoV-2. (23)

Article 1 sought to verify whether myocarditis and myocardial injury were caused by Covid-19. It included 112 patients with clinical data related to the heart, including mainly cardiac imaging findings, laboratory and clinical results. Serial tests of cardiac markers were screened for the analysis of potential myocardial injury/myocarditis. Their results showed evidence of myocardial injury in patients with Covid-19, and 14 (12.5%) patients had abnormalities similar to myocarditis. ⁽²⁴⁾

The clinical evidence from the aforementioned study suggests that myocardial injury is more likely to be related to systemic consequences than to direct damage by Covid-19. The elevation in cardiac markers

probably occurred due to secondary and systemic consequences, and can be considered as a warning sign for recent adverse clinical outcomes of patients. (24)

Article 2 of this review, developed in China, with 1099 patients, showed that at the beginning of the pandemic, the prevalence of coronary artery disease (CAD) in severe and non-severe cases was 5,8%. COVID-19 patients with more severe disease outcomes, under intensive therapy, mechanical ventilation or death, had more underlying CAD than those with a more benign disease course. (25)

The same author reveals that the Covid-19 pandemic has caused major changes in the health system and in the population, including those patients involved in the practice of preventive cardiology. (27) Therefore, early identification, timely and effective treatment, maintenance of hemodynamics and electrophysiological stability are of great importance to alleviate the disease, save lives and ensure a good long-term prognosis. (26)

Article 3 was intended to provide recommendations for a systematic approach to care for patients with AMI during the CO-VID-19 pandemic. He emphasized the importance of primary percutaneous coronary intervention (PCI), as a standard of care, including for confirmed or probable patients with COVID-19. (27)

In addition, patients admitted with acute coronary syndrome who are considered possible carriers of COVID-19, should continue to receive standard medical therapy with early invasive treatment. The authors suggest additional non-invasive diagnosis assessment through risk stratification for CO-VID-19 status, additional assessment for the potential for coronary thrombotic occlusion in relation to other comorbidities. (27)

Published in Canada, article 4 aimed to provide strategies for the management of Heart Failure-HF during the COVID-19 pandemic, and suggests strategies based on virtual care rather than face-to-face, offering consultations through virtual or telehealth. Suggests a virtual assessment of HF as a challenging, but not impossible, initial assessment, requiring the establishment of a clinical and etiological baseline of HF. (28)

With this focus, the virtual consultation between a primary care provider and a specialist with secure messages and two-way communication has been implemented and expanded to also include subspecialty consultation. The study suggests that this type of virtual consultation for primary care providers can be enabled by telephone support or a secure online platform in primary care for patients with HF. (28)

Article 5 referred to the context of populations living in rural areas or remote locations with CVD, where the prevalence is still high. Focused on populations in Australia and New Zealand, some recommendations were suggested during the COVID-19 pandemic, such as having improved access to telehealth consultation for regional and rural outpatients; establish the availability of electrocardiographic reading (ECG) services by a specialist, covering all rural patients uniformly; manage the use of ambulances in these locations, to optimize and transfer patients only when really necessary. (29)

The authors also reinforce the need to guarantee the protection of the team, especially cardiology specialists, with the provision of personal protective equipment (PPE), avoiding reinfection by CO-VID-19; maintain the capacity of rural cardiac care, making changes in regional models, establishing regional pacemaker and defibrillator services, using the supported and technical remote monitoring for the local implantation of these devices. (29)

Article carried out in England (article 6) with 139 people, had as main outcome the delay related to the patient, defined as the time from the onset of symptoms to the first medical contact, without one of the key factors in the pre-hospital care logistics. As the total ischemia time is one of the main determinants of the results in patients with ST segment elevation myocardial infarction and early treatment is essential to reduce morbidity and mortality, a significant delay in medical contact between symptoms and the highest level of Cardiac troponin I on admission to patients during the COVID-19 pandemic may compromise effective care. (30)

More research is needed to understand the various cardiovascular manifestations in patients with COVID-19, in addition to the incidence, mechanisms and clinical presentation of the disease.

More research is needed to understand the various cardiovascular manifestations in patients with COVID-19, in addition to the incidence, mechanisms and clinical presentation of the disease.

As contributions to the health field, the studies identified, although in small numbers, brought very rich information about Covid-19 and cardiovascular disease. He presented current references that point to potentially serious impacts caused by CO-VID-19 on the cardiovascular system, and reinforces the need for adequate monitoring and management of complications. Large centers have built specific recommendations, and the revised scientific production has also brought lines of care for cardiac emergencies associated with CO-VID-19, such as myocarditis and AMI.

CONCLUSION

The disease caused by the new coronavirus represents a wide challenge for the management of infected patients, from supportive treatment, associated complications and monitoring of patients with comorbidities, especially with previous CVD.

This review also highlights the importance of monitoring patients with CVD in chronic treatments, so that the decompensation of the underlying disease does not cause acute events in the critical phase of the infection. In addition, the assertive and systematic control of CVDs must be maintained, since the status of social isolation can interfere with patients' access to health services. The technological resources of telehealth as an ally in combating the pandemic are gaining space in this scenario.

Maintaining health care for patients with CVD is undoubtedly a priority for attention. And studies of greater methodological robustness are needed to produce strong evidence to support the practice.

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