Cogitare Enfermagem

REVIEW

TROPONIN MYOCARDIAL INJURY MARKER AND OUTCOME IN COVID-19: SCOPING REVIEW

HIGHLIGHTS

1. Studies demonstrate troponin changes in patients hospitalized with COVID-19.
2. Elevated troponin has been correlated with increased mortality.
3. There is a need to reduce complications caused by COVID-19.

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ABSTRACT

Objective: To analyze scientific evidence on changes in the myocardial injury marker troponin and clinical outcome in patients hospitalized with COVID-19. **Method:** A scoping review was adopted, in the Medical Literature Analysis and Retrieval System Online, Scientific Electronic Library Online and Virtual Health Library bases, from May to July 2022. Using as descriptors: Troponin; COVID-19; Cardiovascular System. **Results:** 23 studies revealed cardiac alterations in hospitalized patients with COVID-19 by examining the cardio specific biomarker troponin, in addition to relating it to high mortality rates. Studies have shown a great relationship between acute myocardial injury, evidenced by elevated troponin, and a worse outcome during hospitalization. **Conclusion:** Cardiovascular changes were mapped in patients hospitalized with COVID -19 who progressed to severe cases of the disease. This study can contribute to care planning through protocols aimed at clinical management, specific for patients with the disease, both in the acute phase and in the post- COVID -19 phase.

DESCRIPTORS: Troponin; Cardiovascular System; COVID -19; Nursing.

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INTRODUCTION

The first cases of the novel coronavirus emerged in December 2019 in Wuhan, China. Due to the rapid spread of the disease, in March 2020 the World Health Organization declared a pandemic. The virus was classified by the International Committee on Taxonomy of Viruses as SARS-CoV-21. Advanced age group and comorbidities are considered predisposing factors for high lethality rates of COVID -19. Considering this, preventive and informative measures to combat the spread of the disease have been adopted worldwide[2].

The COVID-19 virus, like other respiratory viruses, is transmitted by droplet and aerosol contact. The clinical manifestations caused by SARS-CoV-2 range from asymptomatic and mild, moderate, and severe cases to severe and critical cases, with more severe signs and symptoms requiring special attention as they show worsening clinical evolution and require hospitalizations[3].

The manifestations are like Severe Acute Respiratory Syndrome (SARS). However, studies have shown changes not only in the respiratory system, but also in organs and systems, such as the cardiovascular system. Patients infected with SARS-CoV-2 may develop cardiac pathologies or potentiate existing ones: myocardial lesions, arrhythmias, vascular inflammation, acute myocardial infarction, pulmonary thromboembolism, among others, have already been associated with clinical manifestations of the disease[1].

The literature suggests that cardiovascular injury secondary to the virus may be linked to angiotensin-converting enzyme 2 (ACE2), which is linked to the immune system and present in high concentration in the lung and heart. The virus connects via the spike protein to the ACE2 receptor and enters the host cell, where ACE2 is deactivated, contributing to lung injury. As ACE2 has high concentrations in the heart, possibly severe lesions can occur in this organ[4].

In addition to the inflammatory response, patients infected with the novel coronavirus show changes in inflammatory markers such as D-dimer, ferritin, interleukin-6 (IL-6), lactate dehydrogenase (LDH), C-reactive protein, procalcitonin, leukocyte count and the specific cardiac biomarker Troponin[4].

Troponin, a regulator of muscle contraction, is present in striated and cardiac muscles. It is subdivided into subunits C; I and T. Troponin C (TnC) is directly linked to skeletal muscle fibers and is not considered a marker of specific myocardial injury. Troponins I (TnI) and T (TnT), on the other hand, are directly linked to such injury due to their specific functions[5].

Classified as the gold standard for myocardial injury, troponin can also be evidenced in other clinical conditions, such as myocarditis, electrical cardioversion, cardiac trauma, myositis, pulmonary embolism, and renal failure. Its release occurs gradually in the circulation after cardiomyocyte injury, while in transmural necrosis, release occurs between 2–4 hours after injury, reaching its maximum point around 12 hours; remaining elevated for up to 4–7 days for TnI and 10–14 days for TnT[5].

Since the beginning of the pandemic, health professionals and researchers have spared no effort to unravel the changes and clinical manifestations of COVID-19, and studies are needed to know and describe the main changes in the cardiovascular system. Given this context, there was an interest in identifying the knowledge produced on myocardial injury markers, specifically troponin, in patients with COVID-19.

The objective of this research was to analyze the scientific evidence on changes in the myocardial injury marker troponin and clinical outcome in patients hospitalized with COVID-19.

METHOD

This is a scoping review study, carried out according to the recommendations proposed by the Joanna Briggs Institute, characterized by addressing and reporting on the available evidence on a given topic. The study was conducted in nine stages: title, development of the title and question, introduction, inclusion criteria, search strategy, selection of evidence sources, data extraction, evidence analysis and presentation of results.

To construct the research question, the Population, Concept and Context (PCC) strategy was used, namely: Population: patients hospitalized with COVID-19; Concept: alteration in the troponin marker; Context: hospital care. Based on these definitions, the guiding question was established: what scientific evidence relates the involvement of patients by COVID -19 and the change in the myocardial injury marker troponin?

The bibliographic survey was carried out from May to July 2022, the search period was defined between the years 2019 to 2022. The descriptors used were:" Troponin "," COVID-19" and" Cardiovascular system ", in the databases Medical Literature Analysis and Retrieval System Online (MEDLINE/PubMED), Scientific Electronic Library Online (SciELO) and Virtual Health Library (VHL). The Descriptors in Health Sciences (DeCS) were adopted for Latin American databases and Medical Subject Headings (MeSH) for those in English. Boolean operators were used as shown in Chart 1.

Chart 1 - Search strategies for databases related to the research. Cuiabá, MT, Brazil, 2022

Database	Search strategy
PUBMED	Troponin AND COVID-19 AND Cardiovascular System
MEDLINE	Troponin AND COVID-19 AND Cardiovascular System
SCIELO	Troponin AND COVID-19 AND Cardiovascular System

Source: The authors (2022).

Studies published in Portuguese, English and Spanish with different methodological designs were included. The selected studies that answered the guiding question of this review were read in full, and the references were analyzed for additional studies for potential insertion.

Regarding the relevance of the studies, they were reviewed by two independent researchers and there was no disagreement between them. The level of evidence of the studies that comprised the sample of the present study was not assessed, due to the type of review.

Studies published in Portuguese, English and Spanish with different methodological designs were included. The results extracted corresponded to the design, country, authors, journals, conduct and conclusion, in addition to answering the guiding question of the research, being presented in a table, and discussed in a narrative way.

The Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) was adopted for the selection and inclusion of studies to assist in the decision-making process, according to Figure 1.

The review studies, based on Resolution No. 510 of 2016, do not require approval by the Research Ethics Committee, and the integrity and authorship of the researched documents are guaranteed.

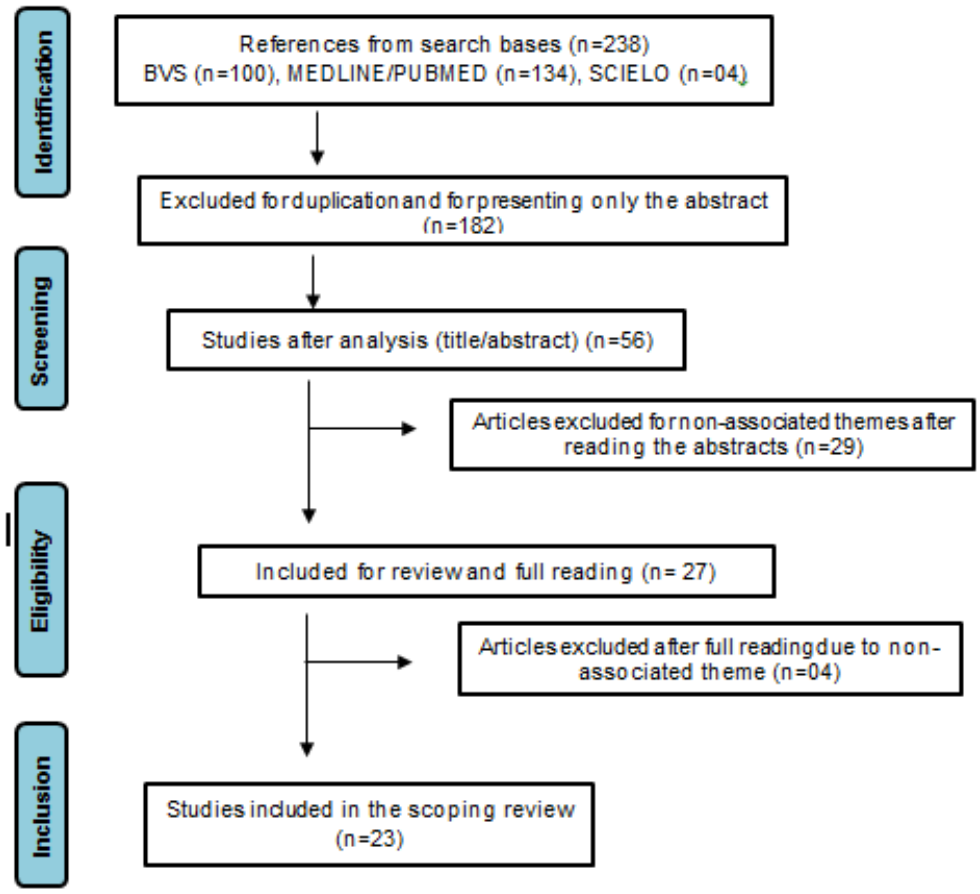

Figure 1 - Flowchart of the search process and summarization of the studies found. Cuiabá, MT, Brazil, 2022

Source: PRISMA Statement; the authors (2022).

RESULTS

A total of 23 studies were included. Regarding the geographical description, the prevalence was in studies conducted in the United States (21.74%). Studies on COVID-19 and troponin elevation demonstrate the importance of the topic, given the severity of the disease and its relationship with changes in this marker. Therefore, the data were extracted and tabulated as shown in Chart 2.

Chart 2 - Characterization of the studies included in the scoping review. Cuiabá, MT, Brazil, 2022

Authors/ Country/ Year	Title	Journal	Design / Sample / Change in troponin and clinical outcome
Alieva, et al[6]. Russia 2022	Prognostic value of cardiac troponins in case of COVID-19.	Therapy	Retrospective Study 48,510 medical records Elevated serum troponin levels were correlated with deteriorating health and increased mortality in patients with and without heart disease. Troponin elevation was associated with death, mechanical ventilation, and intensive care.
Almeida, et al[7]. Brazil 2020	Prognostic Value of Troponin-T and B-Type Natriuretic Peptide in Patients Hospitalized for COVID-19	Arquivos Brasileiros de Cardiologia	Cohort study with convenience sample 183 patients First study in Brazil to identify TnT as an independent predictor of worse prognosis in patients with COVID-19. Troponin elevation was associated with the combined outcome of death or need for mechanical ventilation, with more than half of patients with troponin > 0.03 ng/dl having an unfavorable outcome.
Azevedo, et al[8]. Brazil 2021	*Practical Approach to Acute Coronary Syndrome in Patients with COVID-19*	International Journal of Cardiovascular Sciences	Scoping review 59 studies Acute myocardial injury is significantly associated with in-hospital mortality, with troponin being a marker of worse prognosis in SARS-CoV-2 infected patients. Several studies have shown that myocardial injury, diagnosed by increased troponin levels, is associated with higher mortality in patients with COVID-19.
Bavish, et al[9]. United States 2020	*Acute myocardial injury in patients hospitalized with Covid-19 infection: A review.*	Progress in Cardiovascular Diseases	Review study 26 articles (11,685 patients) Elevation of cardiac biomarkers was found to be common in patients with Covid-19 infection. In this review, the overall prevalence of acute myocardial injury ranged from 5% to 38%. Elevation of cardiac biomarkers, particularly high-sensitivity cardiac troponin (hs-troponin) was considered an important myocardial injury marker for diagnosis and risk stratification.
Cao, et al[10]. China 2020	Myocardial injury and COVID-19: Serum hs-cTnI level in risk stratification and the prediction of 30-day fatality in COVID-19.	Theragnostic	Review study 26 articles (11,685 patients) Elevation of cardiac biomarkers was found to be common in patients with Covid-19 infection. In this review, the overall prevalence of acute myocardial injury ranged from 5% to 38%. Elevation of cardiac biomarkers, particularly high-sensitivity cardiac troponin (hs-troponin) was considered an important myocardial injury marker for diagnosis and risk stratification.
Carillo-Esper, et al[1]. Mexico 2020	Manifestaciones extrapulmonares de la infección por SARS-CoV-2.	Cirugía Y Cirujanos	Theoretical study Cardiac biomarker studies suggest a high prevalence of cardiac injury in patients hospitalized for Covid-19, with myocardial injury being an important prognostic factor.

Case, et al[11]. United States 2021	Clinical impact and predictors of troponin elevation in patients with Covid-19	Cardiovascular Revascularization Medicine	Cohort study 2,716 patients with Covid-19 Of the sample, 250 had troponin elevation, presenting a higher risk for mechanical ventilation. Hospital mortality was significantly higher (48.4%) in COVID-19 positive patients with troponin elevation than without troponin elevation (12.2%; p<0.001).
Chen, et al[12]. . China 2020	*Cardiovascular manifestations in severe and critical patients with COVID-19.*	Clinical Cardiology	Incidence study 54 patients with COVID-19 Troponin elevation was observed in 23 (42.6%) patients, with three patients having highly elevated values (>3 times the upper reference limit), indicative of severe myocardial injury, and all being classified as critical cases.
Fan, et al[13]. China 2019	Risk factors for myocardial injury in patients with coronavirus disease 2019 in China.	Esc Heart Failure	Cohort study 353 patients with COVID-19 Of the sample, 79 patients had myocardial injury. High troponin levels were significantly associated with immune response, multiple organ dysfunction and poor outcomes.
Kaufmann, et al[14]. Austria 2022	*Biomarkers Associated with Cardiovascular Disease in COVID-19.*	Cells	Theoretical study The prognostic value of troponin in COVID-19 patients has been consistently demonstrated in several different study populations worldwide and has been confirmed by data from several meta-analyses. In the case of myocardial injury, a clear correlation with symptoms and signs of myocardial ischemia (chest pain, ECG, and echocardiogram) is necessary to adequately guide management decisions.
Kavsak, et al[15]. Canada 2021	Cardiac Troponin Testing in Patients with COVID-19.	Clinical Chemistry	Theoretical study After respiratory complications, cardiac complications were the most prevalent finding in COVID-19 patients. Increased troponin (based on a threshold of 28 ng/L) at hospital admission may have a greater association with death.
Lala, et al[16]. United States 2020	Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection	Journal of the American college of cardiology	Cohort study 3,069 patients hospitalized with Covid-19 Myocardial injury reflected by troponin concentrations above the upper reference limit of 0.03 ng/ml was present in 36% of patients hospitalized with COVID-19. Troponin levels among patients were generally <1.0 ng/ml. Even small amounts of myocardial injury (for example) troponin I >0.09 ng/dl, n = 530 [19.4%]) were associated with a more pronounced risk of death.
Luchian, et al[17]. Bélgica 2021	Troponin T in COVID-19 hospitalized patients: Kinetics matter	Cardiology Journal	Prospective study 202 patients Elevated cardiac troponin T on admission was associated with increased in-hospital mortality, whereas patients with troponin levels within the standards had less cardiovascular changes. The study emphasizes the additional role of cTnT testing in COVID-19 patients for risk stratification and improved diagnostic and management pathway.

Majure, et al[18]. United States 2021	Usefulness of Elevated Troponin to Predict Death in Patients With COVID-19 and Myocardial Injury	The American Journal of Cardiology	Analytical study 6,247 hospitalized patients with Covid-19 Of the sample, 4426 (71%) patients had normal troponin result, 919 (15%) mildly elevated and 902 (14%) had severely elevated troponin. Patients hospitalized with COVID-19 and elevated troponin had markedly increased mortality compared with patients with normal troponin levels. This risk was independent of cardiovascular comorbidities and elevated markers of inflammation.
Marzo, et al[19]. Italia 2021	Prevalence and prognostic value of cardiac troponin in elderly patients hospitalized for COVID-19.	Journal of Geriatric Cardiology	Retrospective study 343 patients Of the sample, 88 (25.7%) had troponin results above the upper reference limit (0.046 μg/L). Patients with elevated troponin had more comorbidities, greater impaired respiratory exchange, and higher inflammatory markers on admission than those with troponin levels within standards. In addition, they died more (73.9% vs. 37.3%, P < 0.001) over 15 (6-25) days of hospitalization.
Nascimento, et al[20]. Brazil 2020	Troponina Cardíaca como Preditor de Injúria Miocárdica e Mortalidade por COVID-19	Arquivos Brasileiros de Cardiologia	Editorial. Myocardial injury is not uncommon in patients with COVID-19, and elevated cardiac troponin is a predictor of in-hospital mortality. The measurement of cTnI throughout hospitalization can facilitate the risk classification of these patients, with the advantage of being an easily reproducible method.
Rezabakhsh, et al[21]. Iran 2022	A close-up view of dynamic biomarkers in the setting of COVID-19: Striking focus on cardiovascular system.	Journal of Cellular Molecular Medicine	Theoretical study Some evidence has suggested that a significantly high rate of cTnI induced by cardiac dysfunction could be considered an independent predictor of mortality from Covid-19. Troponin results could be applied for risk stratification on admission and assessment of disease progression in hospitalized patients.
Sahranavard, et al[22]. Iran 2021	Cardiac Complications in COVID-19: A Systematic Review and Meta-analysis	Archives of Iranian Medicine	Systematic review 22 articles included Comparisons of troponin levels between survivors and patients who died were performed in four studies, and the results showed that patients who died had higher troponin levels compared to survivors.
Shafi, et al[23]. England 2020	Cardiac manifestations in COVID‐19 patients - A systematic review	Journal of Cardiac Surgery	Systematic review 61 articles included A wide range of cardiac manifestations are associated with the interaction between Covid-19 and the cardiovascular system. Specific cardiac biomarkers, such as troponin, provide a useful prognostic tool to help identify patients with severe disease early and allow timely treatment escalation.

Shah, et al[24]. United States 2020	Prognostic Value of Elevated Cardiac Troponin I in Hospitalized Covid-19 Patients	American Journal of Cardiology	Retrospective study 635 medical records of patients with Covid-19 In 309 patients, troponin I was measured at least once during hospitalization. Of these patients, 116 (37.5%) had elevated troponin I, and were found to have a higher need for intubation, dialysis, and ICU transfer. In addition, overall mortality was significantly higher among patients with elevated cTnI.
Sharma, et al[25]. India 2021	Cardiovascular manifestations of COVID-19: An evidence-based narrative review	Indian Journal of Medical Research	Theoretical study Troponin elevation is associated with increased incidence of malignant arrhythmias and mortality from Covid-19. In the initial report from Wuhan, China, up to 27.8% of Covid-19 patients had an elevated troponin level, indicating myocardial damage during hospitalization.
Tersalvi, et al[26]. Switzerland 2020	Elevated Troponin in Patients with Coronavirus Disease 2019: Possible Mechanisms	Journal of Cardiac Failure	Theoretical study Elevated troponin levels are frequent in Covid-19 patients and significantly associated with fatal outcomes. Several mechanisms may explain this phenomenon: viral myocarditis, cytokine-induced myocardial injury, microangiopathy and unmasked coronary artery disease.
Tuo, et al[3]. China 2021	Cardiac Biomarker Abnormalities Are Closely Related to Prognosis in Patients with COVID-19	International Hearth Journal	Observational study 148 patients The incidence of cardiovascular complications happened in 19 patients (12.8%). Five of them were survivors (5.2%) and 14 of them were non-survivors (26.9%). Compared to survivors, non-survivors had higher levels of high-sensitivity cardiac troponin I.

Source: The authors (2022).

The studies show a concordant relationship with each other regarding troponin changes in hospitalized patients with COVID-19. Elevated serum troponin levels were correlated with deterioration in health and increased mortality in patients with and without heart disease. Troponin elevation was associated with death, mechanical ventilation and intensive care[6,24].

A wide range of cardiac manifestations are associated with the interaction between COVID-19 and the cardiovascular system. Specific cardiac biomarkers, such as troponin, provide a useful prognostic tool to help identify patients with severe disease early and allow timely treatment escalation[17,21,23]

DISCUSSION

Studies have shown a great relationship between acute myocardial injury, evidenced by elevated troponin in patients hospitalized for COVID-19 and a worse outcome during hospitalization. In this case, individuals who presented changes in the marker require intensive care, in the vast majority, which is a predictor of higher lethality in patients infected with COVID-19[1,8,10,12,15-18,22,24,26].

A study carried out with 296 patients in intensive care beds with COVID-19, with the objective of evaluating the prevalence of elevated cardiac troponin levels relating the ability of this marker to predict mortality within 60 days, showed a high prevalence of troponin I elevation in these patients, and those who died showed higher elevation values[27].

Corroborating this finding and the results of this review, a study showed that 20 to 30% of patients hospitalized with COVID-19 had myocardial injury manifested by troponin elevation, also identifying that ventricular arrhythmias were more frequent in patients with elevation of this marker. The authors also observed that cardiac injury was linked to a worse prognosis of COVID-19, greater need for mechanical ventilation and higher mortality rates. In COVID-19 survivors with cardiac injury, the authors suggest that appropriate clinical trials be conducted to correctly identify such problems and plan appropriate care for the long-term sequelae of post-COVID-19 cardiac syndrome[28].

In line with these findings, in another study that sought to identify the relationship between COVID-19 and the damage the disease could cause to the heart muscle, it was observed that the main cardiovascular complications of post-acute Covid-19 syndrome were atrial and ventricular arrhythmias and bradyarrhythmias. It was related that high mortality and morbidity rates were higher for patients with myocardial lesions. It was also found that there is a direct relationship between COVID -19 and cardiac injury. Thus, the authors consider cardiac follow-up relevant for patients surviving COVID -19, especially those known to have elevated cardiac troponin during hospitalization[29].

An observational cohort study conducted at a University Hospital in Frankufrt in April 2020 already sought to assess the presence of myocardial injury in patients recently recovered from Covid-19. These patients underwent cardiac blood markers and Cardiovascular Magnetic Resonance Imaging (CMRI), which indicated that troponin T was detectable in more than 70% of patients. In addition, ejection fraction was decreased and left ventricular enlargement was observed. Regarding CMR (Cardiovascular Magnetic Resonance), 78% of patients recovered from COVID-19 had abnormal findings, such as increased native T1 of the myocardium[30].

These studies corroborate the other results already described in this study, and cardiovascular involvement is evident both in the acute phase of COVID-19 and post COVID-19.

Regarding the limitations of the study, it is emphasized that the sources of evidence are still insufficient, as the information is unlimited and may undergo new approaches as new scientific findings emerge. In addition, the results demonstrated in this study still follow a specifically medical approach bias, with little inclusion of other professions, such as nursing, which represents a fundamental and essential part for the management and clinical approach to patient care in hospital units.

FINAL CONSIDERATIONS

The search for evidence related to the objective of this study was achieved, considering the availability of articles in databases, thus enabling greater depth regarding troponin changes and elevations in hospitalized patients with COVID-19.

Most studies have shown a high mortality rate in patients with altered levels of the cardiac marker troponin, related to a greater chance of hospitalization in an intensive care bed, use of mechanical ventilation and death. Thus, monitoring biomarkers since the patient's admission will allow a specific care plan to be carried out with the objective of a better prognosis, considering the predisposition of patients affected by COVID-19 to evolve to more severe conditions of the disease or death. The need for follow-up care for patients surviving the disease is also highlighted.

The need to reduce the complications caused by COVID-19 is a professional and scientific challenge, regarding nursing, it can be highlighted that the development of studies such as this one contributes to care planning through the creation of care protocols aimed at specific care and clinical management for patients infected with the disease, both in the acute phase and in the post-COVID-19 phase.

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Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - **Rodrigues AA, Cenzi CM**. Drafting the work or revising it critically for important intellectual content - **Rodrigues AA, Cardoso JDC, Miraveti J de C, Cenzi CM.** Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - **Rodrigues AA, Cardoso JDC, Miraveti J de C, Cenzi CM**. All authors approved the final version of the text.

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