

Review

Incidence and Prevalence of Myocarditis in COVID-19 Infections

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Abstract

The outbreak of COVID-19, caused by a novel virus, has led to a global pandemic with significant implications for public health. COVID-19 exhibits a wide range of manifestations, affecting multiple organs in addition to the respiratory system. Cardiovascular complications, including myocarditis, have been observed in a substantial proportion of hospitalized COVID-19 patients and are associated with adverse outcomes. Studies have reported varying rates of myocarditis incidence among COVID-19 patients, with seasonal variations and higher numbers observed in the summer. The relative numbers of myocarditis cases are highest in younger individuals, but the in-hospital case-fatality rate increases with age. COVID-19 patients with myocarditis are more likely to require intensive care and ventilation support. Myocarditis is independently associated with increased case-fatality and the occurrence of venous thromboembolism in COVID-19 patients. Understanding the incidence and prevalence of myocarditis in COVID-19 is essential for patient management and prognosis.

Keywords: COVID-19, myocarditis, cardiovascular complications, incidence, prevalence

Introduction

The outbreak of a previously unknown virus causing pneumonia was first detected in Wuhan, China in December 2019 (1). The COVID-19 pandemic, declared by the World Health Organization in 2020, has impacted millions of individuals globally (2). COVID-19 exhibits a wide range of manifestations, from asymptomatic infection to severe multi-organ failure and mortality. While the respiratory system is primarily affected, there is a growing recognition of additional complications involving multiple organs (3).

COVID-19 commonly presents with symptoms such as fever, cough, sore throat, fatigue, muscle pain, and difficulty breathing. The infection primarily affects the lungs and can lead to pneumonia, respiratory failure, and other lung-related complications (4, 5). In addition to the lungs, COVID-19 can also cause acute damage to the heart, kidneys, and liver. COVID-19 is associated with a diverse array of cardiovascular complications, such as myocarditis, acute myocardial infarction, heart failure, life-threatening arrhythmias, and cardiogenic shock. These cardiovascular manifestations have been observed in approximately 20-30% of hospitalized COVID-19 patients and are linked to unfavorable outcomes (6, 7). According to several studies, myocardial injury is a frequent occurrence among COVID-19 patients who develop cardiovascular complications, comprising approximately 7% to 23% of cases. This myocardial injury has been associated with increased rates of morbidity and mortality (8). Another study reported cardiac injury in hospitalized patients ranging from 7% to 17% (9, 10).

The exact mechanism underlying cardiovascular complications in COVID-19 remains uncertain, but it is believed to be a result of a combination of factors. This includes both direct viral injury to the heart and surrounding tissues (myo-pericardium) as well as the inflammatory cytokine storm. The virus is thought to utilize angiotensin-converting enzyme-2 (ACE2) receptors present in cardiac tissue, triggering an inflammatory response and

intensifying the cytokine storm characteristic of COVID-19 (11).

Prior to the COVID-19 pandemic, the estimated global incidence of myocarditis ranged from 1 to 10 cases per 100,000 people per year, with the highest risk among individuals aged 20 to 40. The use of cardiac MRI has increased in recent years, leading to higher detection rates of myocarditis in the United States (12). During the COVID-19 pandemic, a multicenter study involving various European countries and the US reported a prevalence of myocarditis ranging from 2.4 to 4.1 cases per 1000 hospitalized patients with COVID-19 (13). Another study conducted in Germany found a low burden of myocarditis cases among COVID-19 patients in 2020, but those with both myocarditis and COVID-19 had a significantly higher in-hospital mortality rate compared to those with myocarditis alone (14).

In this review, we will discuss the current understanding of incidence and prevalence of myocarditis in patients with COVID-19 infection.

Methodology

To conduct this study, an extensive literature search was carried out on June 5, 2023, using the Medline and Cochrane databases. The search incorporated medical topic headings (MeSH) and a combination of relevant terms available within the databases. The focus was on articles published between 2020 and 2023, aiming to gather the most current information. In order to ensure a comprehensive review, a manual search was also performed using Google Scholar, building upon previously identified papers. The review encompassed articles discussing COVID-19 infection and its cardiac complications, myocarditis incidence and prevalence. To maintain inclusiveness, no restrictions were placed on publication type, participant age, language, or publication date.

Discussion

COVID-19 infection is correlated with a broad range of cardiovascular complications, including myocarditis, acute myocardial infarction, heart failure, life-threatening arrhythmias, and cardiogenic shock. These cardiovascular

manifestations have been identified in approximately 20-30% of COVID-19 patients who require hospitalization, and they have been associated with adverse outcomes (6, 7). Myocarditis, an inflammation of the heart muscle, has been recognized as one of the most frequent cardiovascular complications associated with COVID-19 infection. Understanding the incidence and prevalence of myocarditis in COVID-19 is crucial for assessing its impact on patients and informing clinical management strategies.

Acute myocarditis, irrespective of the cause, has an estimated annual incidence of around 22 cases per 100,000 individuals in the general population. Among these cases, heart failure (HF) develops in approximately 0.5% to 4.0% of individuals (15). Determining the true prevalence of myocarditis specifically in COVID-19 patients presents challenges due to initial reports lacking specific diagnostic methods to assess myocarditis and the presence of circulating biomarkers that may indicate myocardial injury but can also be associated with non-primary myocardial damage such as multiorgan failure, hypoxia, hypoperfusion, and activation of hemostasis (16).

Several studies have investigated the occurrence of myocarditis in COVID-19 patients, but the reported rates have varied across different populations and research settings. A multicenter study conducted in Europe and the United States aimed to determine the prevalence of myocarditis among patients hospitalized with COVID-19. The study reported a prevalence ranging between 2.4 cases of definite or probable myocarditis and 4.1 cases of definite, probable, or possible myocarditis per 1000 hospitalized COVID-19 patients (13). These findings highlight that myocarditis can be a notable complication in COVID-19 cases.

Another study conducted in Germany focused on the incidence of myocarditis in hospitalized COVID-19 patients. The study revealed several important findings regarding myocarditis in hospitalized COVID-19 patients. The incidence of myocarditis was found to be 1.28 cases per 1000 hospitalizations, indicating its occurrence as a

notable complication. Seasonal variations were observed, with higher numbers of myocarditis cases during the summer. The relative numbers of myocarditis cases were highest among individuals in the first two decades of life, but the in-hospital case-fatality rate increased significantly with age. COVID-19 patients with myocarditis had a higher likelihood of requiring ICU admission and ventilation treatment. The in-hospital case-fatality rate was 1.36 times higher in COVID-19 patients with myocarditis compared to those without myocarditis. Myocarditis was independently associated with a 1.5-fold increase in case-fatality, regardless of age, sex, and comorbidities. Additionally, it was linked to a 2.8-fold increase in the occurrence of venous thromboembolism. Factors such as age below 70 years, male sex, coronary artery disease, heart failure, pneumonia, and multisystemic inflammatory COVID-19 infection were independently associated with myocarditis in COVID-19 patients (17). These findings suggest that the presence of COVID-19 in patients with myocarditis may contribute to a poorer prognosis.

In the United States, the Center for Disease Control and Prevention (CDC) reported a notable increase in myocarditis cases among hospitalized patients during 2020 compared to the previous year. According to their analysis of a hospital-based administrative database, there was a 42.3% rise in myocarditis incidence (18). It is important to interpret these findings in the context of increased awareness, testing, and reporting of myocarditis during the COVID-19 pandemic, which may have contributed to the observed increase.

Overall, multiple studies indicate that myocardial injury is observed in a significant proportion of severe COVID-19 pneumonia cases, ranging from 15% to 27.8% (6, 19, 20). Notably, COVID-19-related myocarditis has been reported in patients who did not initially present with pneumonia, suggesting the potential for delayed onset of cardiovascular complications, even in individuals with mild symptoms (21). Furthermore, diffuse myocardial injury has been detected in early-stage

COVID-19-recovered patients who did not exhibit active cardiac symptoms (22).

It is worth noting that the diagnosis of myocarditis in COVID-19 patients can be challenging. Myocardial injury can result from direct viral injury to the heart muscle and surrounding tissues (myopericardium), as well as from the exaggerated immune response and inflammatory cytokine storm triggered by the virus. The exact mechanisms and contributions of these factors to the development of myocarditis in COVID-19 are still being studied.

To investigate the prevalence and impact of myocarditis in COVID-19, advanced imaging techniques such as cardiovascular magnetic resonance (CMR) imaging have been utilized. CMR provides detailed information about cardiac structure, function, and tissue characterization, aiding in the diagnosis and assessment of myocardial inflammation. A study assessing CMR findings in patients recently recovered from COVID-19 reported cardiac involvement, including myocarditis, in 78% of the patients (23). These findings further emphasize the significance of myocardial injury in COVID-19 and its potential long-term consequences.

While the mentioned studies provide insights into the incidence and prevalence of myocarditis in COVID-19 infection, it is important to recognize that research on this topic is continuously evolving. Ongoing studies are essential for obtaining a comprehensive understanding of the true burden of myocarditis in COVID-19, as well as its clinical implications and long-term outcomes.

Conclusion

Myocarditis is recognized as a potential cardiovascular complication in COVID-19 patients. The reported incidence and prevalence of myocarditis in COVID-19 have varied across different populations and studies. However, evidence suggests that myocarditis can occur in a significant proportion of hospitalized COVID-19 patients and is associated with increased morbidity and mortality. Continued research is necessary to elucidate the underlying mechanisms, risk factors,

and long-term implications of myocarditis in the context of COVID-19.

Disclosure

Conflict of interest

There is no conflict of interest

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Ethical consideration

Non applicable

Data availability

Data that support the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

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