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Cardiovascular Disorders as a Risk Factor for Severe Covid-19: A Systematic Literature Review

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Abstract

Objectives

This systematic review examined the relationship between cardiovascular disorders and severe COVID-19 outcomes. The study aimed to quantify the extent to which individuals with cardiovascular disorders are at risk of developing severe COVID-19 compared to those without these conditions.

Methodology

A comprehensive search was conducted across PubMed, ScienceDirect, Google Scholar, and the Cochrane Library databases. Keywords used included "COVID-19," "SARS-CoV-2," "coronavirus," "cardiovascular disorders," "hypertension," "coronary artery disease," "heart failure," "atrial fibrillation," "risk factor," and "severe." The search was limited to articles published between 2020 and 2023 and written in English. The quality of the studies was assessed using the Newcastle-Ottawa quality assessment tool.

Results

An initial search identified 3,059 studies (Google Scholar = 1,073; ScienceDirect = 752; PubMed = 1,234). After applying the eligibility criteria, 37 articles were selected for inclusion. Individuals with cardiovascular disorders were found to be significantly more likely to experience severe COVID-19 outcomes, with an odds ratio (OR) of 1.88 (95% CI: 1.32–2.70) for hospitalization and an OR of 3.576 (95% CI: 1.694-7.548) mortality.

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The most commonly studied cardiovascular disorders were hypertension, coronary artery disease (CAD), heart failure (HF), and atrial fibrillation, all of which were associated with increased rates of ICU admission and mechanical ventilation.

Conclusion

These findings underscore the need for heightened surveillance and management of individuals with cardiovascular disorders during the COVID-19 pandemic. The inclusion of a dedicated statistician is recommended to enhance the statistical rigor of future research. Further investigations are necessary to elucidate the mechanisms by which cardiovascular disorders contribute to severe COVID-19 outcomes and to develop targeted strategies for risk mitigation.

Keywords

COVID-19; SARS-CoV-2; Hypertension; Cardiovascular disorders; Coronary artery disease; Heart failure.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has been associated with a diverse range of clinical manifestations among affected individuals. While some patients remain asymptomatic or exhibit mild symptoms, others may experience severe disease characterized by widespread inflammatory responses, microvascular injury, and coagulopathy [1]. The risk of developing cardiovascular complications due to COVID-19 is notably increased in individuals with preexisting cardiovascular risk factors, including advanced age, hypertension, obesity, diabetes, and atherosclerosis, which are indicative of compromised endothelial function [2]. The infection can exacerbate these preexisting conditions, leading to complications such as inflammation, thrombosis, and microvascular obstruction, potentially resulting in multi-organ dysfunction, including myocardial injury, irrespective of the presence of epicardial coronary artery disease (CAD) [3].

Cardiovascular manifestations of COVID-19 are heterogeneous and may include a variety of conditions such as thrombosis (arterial, venous, and pulmonary), arrhythmias (both atrial and ventricular), heart failure (HF), and shock [4]. These complications have been associated with significantly elevated mortality rates, underscoring the critical need for vigilant monitoring of patients with preexisting cardiovascular diseases. The profound impact of COVID-19 on the cardiovascular system highlights the increased risk for individuals with underlying cardiovascular conditions to develop severe complications. The recognition of the multifaceted nature of cardiovascular presentations in COVID-19, alongside the necessity for careful monitoring, emphasizes the urgent need for further research to elucidate underlying mechanisms and to develop targeted interventions aimed at mitigating the risk of severe cardiovascular complications in affected individuals [5]. Notably, right ventricular dilation has been observed in hospitalized patients with COVID-19, further complicating the clinical picture [6]. The primary objective of this systematic literature review is to assess cardiovascular disorders (CVD) as a risk factor for severe COVID-19.

Objectives

This review aims to investigate cardiovascular disorders—including hypertension, HF, arrhythmias, thrombosis, myocardial injury (myocarditis), acute coronary syndrome, and ischemic heart disease

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(IHD)—as risk factors for severe COVID-19. Severe COVID-19 is defined as cases requiring hospitalization, intensive care unit (ICU), mechanical ventilation, or resulting in mortality.

Methodology

Inclusion criteria

Studies selected for inclusion met specific criteria. They had to be observational or interventional, encompassing case-control studies, cohort studies, and randomized controlled trials. Only studies involving adult human participants diagnosed with cardiovascular disorders, such as hypertension, CAD, HF, or atrial fibrillation (AF), were included. Outcomes of interest pertained to severe COVID-19, defined as cases requiring hospitalization or ICU admission, as well as mechanical ventilation and mortality. Eligible studies were published between 2020 and 2023, in English, and appeared in peer-reviewed journals with full-text availability. Preference was given to studies published in high-impact journals exhibiting a low risk of bias, as assessed through quality evaluation. Studies explicitly addressing the relationship between cardiovascular disorders and severe COVID-19 were prioritized, excluding those focused solely on general COVID-19 outcomes.

Exclusion criteria

Exclusion criteria comprised basic science studies, animal studies, in vitro studies, and studies involving pediatric participants or those without diagnosed cardiovascular disorders. Additionally, studies reporting outcomes unrelated to severe COVID-19—such as general infection or symptom severity—were excluded. Unpublished works, books, newspapers, case studies, dissertations, literature reviews, narrative articles, theses, and grey literature were also omitted from consideration.

Search strategy

A comprehensive search was conducted using PubMed, Google Scholar, and ScienceDirect databases. The search utilized a combination of keywords and Boolean operators, including "COVID-19," "SARS-CoV-2," "cardiovascular disorders," and "risk factor." Truncation and wildcard symbols were employed to capture articles with varying word forms of the keywords. The search was restricted to articles published from 2020 to 2023, in English, and focused on observational or interventional studies. Keywords were combined strategically to enhance search results, with data runs conducted individually for each database followed by a combined review.

Study selection process

The combined search results were imported into the Zotero application, where duplicate entries were identified and removed. The titles and abstracts of the non-duplicate articles were screened for relevance to the topic. Full-text articles were subsequently evaluated for eligibility based on the established inclusion and exclusion criteria. Eligible articles were included in the systematic review, and references of these articles were also scrutinized for additional potential sources.

Assessment of Methodological Quality

The methodological quality of the included studies was assessed to ensure a low risk of bias. The Newcastle-Ottawa Scale was utilized for this evaluation, which assesses studies based on three main

components: selection of study groups, comparability of groups, and ascertainment of exposure or outcome of interest. Each component was evaluated against specific criteria, with scores assigned accordingly.

Search Terms and Strings

Search terms

1. COVID-19
2. SARS-CoV-2
3. Coronavirus
4. Cardiovascular disorders
5. Hypertension
6. Coronary artery disease
7. Heart failure
8. Atrial fibrillation
9. Risk factor
10. Severe
11. Hospitalization
12. Intensive care unit
13. Mortality

Search strings

Table 1: Search Strings

Filters

- Publication Date: 2020 - 2023
- Language: English
- Study Design: Observational OR Interventional OR Case-Control OR Cohort OR Randomized Controlled Trial OR Systematic Review OR Meta-Analysis.

Results

Search results

The initial search yielded a total of 3,059 studies (Google Scholar: 1,073; ScienceDirect: 752; PubMed: 1,234). Following a title and abstract screening, 2,562 studies were assessed, with 1,725 excluded due to irrelevance to the topic. A total of 837 studies were selected for full-text review, resulting in the retrieval of 266 articles. Out of these, 234 articles were excluded for failing to meet the inclusion criteria. Ultimately, 32 articles from the study selection process, along with 5 articles identified through reference searching, were incorporated into this systematic literature review. The PRISMA flowchart (Figure 1) illustrates the study selection process for the database articles.

Quality assessment: newcastle ottawa scale

The quality assessment, summarized in Table 2, evaluated 37 studies using the Newcastle-Ottawa Scale. Most studies received a score of 7, indicating moderate quality. This score reflects certain

methodological strengths, including well-defined exposed cohorts and clear outcome measures, but also highlights areas needing improvement, such as the selection of non-exposed cohorts and the control of significant prognostic factors. Notably, three studies [8,38, 39], achieved a score of 9, showcasing superior methodological rigor, comprehensive data collection, and robust comparability between exposed and non-exposed groups.

Characteristics of included studies

Table 3 outlines the characteristics of the included studies, while Figure 2 depicts the prevalence of hypertension and IHD. The studies comprised various designs: randomized controlled trials (RCTs) [8, 38, 40], cohort studies [39, 42, 43], retrospective studies [9-37, 41], and one epidemiological study [44].

Results of included studies

In study [37], cardiovascular diseases emerged as significant predictors of COVID-19 hospitalization, presenting an odds ratio (OR) of 1.88 (95% CI: 1.32–2.70). Hypertension was identified as the most prevalent cardiovascular condition among hospitalized COVID-19 patients across multiple studies [8], [29] - [31], [34], [36], [40], [44]. The prevalence of hypertension varied significantly, ranging from 15% [9], [27] to as high as 77% [34]. Study [28] reported an elevated risk of mortality among hypertensive patients, with an OR of 3.576 (95% CI: 1.694–7.548).

In a comparative analysis, study [13] divided its cohort into a deceased group and a recovered group, revealing that the deceased group had a higher prevalence of hypertension (36.7% vs. 15.5%, $P < 0.001$). Similarly, 73.4% of deceased patients in study [27] were hypertensive. Study [27] indicated that deceased patients exhibited a greater prevalence of hypertension (52%) compared to those who were discharged (37%). Univariate logistic regression in study [26] illustrated significant associations between hypertension and outcomes such as ICU admission (OR=2.4, 95% CI: 1.2–4.5), intubation (OR=2.8, 95% CI: 1.1–7.0), and death (OR=2.8, 95% CI: 1.4–5.5). Study [44] found hypertension to be associated with an OR of 1.49 (95% CI: 1.10–2.01) for critical COVID-19 and OR=1.30 (95% CI: 0.94–1.79) for fatal COVID-19. The proposed mechanisms linking hypertension to COVID-19 severity include increased susceptibility to viral entry, immune dysregulation, and the presence of comorbidities [10], [26] - [28].

Cerebrovascular disease was also identified as a risk factor for severe COVID-19. Univariate logistic regression in study [26] showed cerebrovascular disease significantly correlated with ICU admission (OR=1.9, 95% CI: 1.3–3.0), intubation (OR=3.2, 95% CI: 1.6–6.4), and death (OR=4.5, 95% CI: 2.5–8.0).

Several studies reported varying prevalence rates of ischemic heart disease among COVID-19 patients, ranging from 7.28% to 38% [8], [17], [18], [27], [28], [29] - [32], [34], [42]. The link between IHD and severe COVID-19 can be attributed to compromised cardiovascular function and reduced physiological reserves during viral infection.

Additional cardiovascular conditions associated with severe COVID-19 included ventricular arrhythmia [8], heart disease [10], [17], [18], HF [8], [14], [30], [44], cardiac injury [10], [15], and atrial fibrillation [10], [41]. In a comparison between recovered and deceased groups, study [10] found a higher prevalence of

heart disease among the deceased (11.9% vs. 3.4%, P=0.031). Study [26] highlighted existing CAD as a significant predictor of ICU transfer or mortality, while multivariable Cox regression analysis in study [27] revealed a hazard ratio of HR=1.855 (95% CI: 1.006–3.421; P=0.048) for COVID-19 hospitalization. Similarly, study [26] indicated that deceased patients exhibited a higher prevalence of HF (49%) compared to the recovery group. In study [30], HF was independently associated with acute in-hospital mortality (OR=9.75; 95% CI: 1.95–48.65), and study [44] reported HF to be associated with an OR of 2.13 (95% CI: 1.12–4.05) for critical COVID-19 and OR=1.94 (95% CI: 0.99–3.77) for fatal COVID-19.

Study [26] indicated that acute cardiac injury was present in 77% of deceased patients compared to those who recovered. In multivariate analysis, study [29] identified cardiac injury on admission as an independent predictor of mortality, with an OR of 10.58 (95% CI: 2.42–46.27; P < 0.001). Atrial fibrillation [30] was associated with ICU admission (OR=4.68; 95% CI: 1.66–13.18) and increased in-hospital mortality risk (OR=1.05; 95% CI: 1.02–1.09). The prevalence of these cardiovascular conditions varied across studies, underscoring the need for further research into their specific impacts on COVID-19 outcomes.

ICU admission rates among individuals with cardiovascular disorders ranged significantly from 0.7% [28] to 69% [11]. Notably, both studies investigated hypertension as a cardiovascular condition within hospitalized populations. This substantial variability suggests that additional factors beyond cardiovascular disease may influence clinical outcomes.

Mortality rates among COVID-19 patients with cardiovascular disorders varied from 2.9% [29] to 48.9% [39]. The higher mortality rates in this population highlight the urgent need to address cardiovascular health in the context of COVID-19 management. The interplay between COVID-19 and pre-existing cardiovascular conditions can lead to exacerbated complications and poorer patient outcomes.

In addition to individual studies, large-scale cohort studies encompassing millions of participants corroborated the association between cardiovascular disorders and severe COVID-19. These studies demonstrated elevated hospitalization, ICU admission, and mortality rates among individuals with cardiovascular conditions compared to their counterparts without such conditions.

The hospitalization and ICU admission rates in the RCT study [8] were uniformly 100%. In contrast, retrospective studies exhibited hospitalization rates ranging from 24% to 100%, and ICU admission rates fluctuated between 0.7% and 69%. The participant numbers across these studies varied from 63 to 5,279, revealing no clear correlation between participant count and hospitalization or ICU rates. Studies with the largest participant numbers often reported a 100% hospitalization rate, while the study with the smallest cohort also reflected this trend. ICU admission rates in larger studies ranged from 11% to 32%, whereas smaller studies showed a wide variation from 0.7% to 69%.

Discussion

The recent COVID-19 pandemic has illuminated the intricate relationship between infectious diseases and comorbid conditions [45]. Numerous studies have indicated that individuals hospitalized for COVID-19 frequently have underlying conditions such as hypertension, cardiovascular diseases, and IHD. These comorbidities are well-known to heighten the risk of disease progression and mortality in COVID-19

patients. Upon hospitalization, affected individuals often exhibit biomarkers indicative of cardiac stress or injury, along with elevated levels of inflammation [49]. This physiological response, combined with the virus's direct effects, has led to a higher incidence of cardiovascular complications, including arrhythmias, HF, and thrombotic events.

According to the Cochrane Heart Group, the mechanisms by which COVID-19 may precipitate and exacerbate cardiovascular complications stem from the severe inflammatory response triggered by the virus, as well as the acute respiratory distress syndrome that can induce hypoxia and diminish myocardial oxygen delivery [47]. These mechanisms, particularly when present in individuals with preexisting IHD, significantly increase the risk of adverse cardiovascular outcomes.

Data indicate that hypertension poses a more substantial risk factor for COVID-19 patients compared to other cardiovascular conditions. Several factors contribute to this high prevalence: hypertension affects approximately one in three adults worldwide, making it likely that a considerable portion of those infected with COVID-19 also has this condition. Additionally, hypertension has been associated with an increased risk of severe illness and mortality from COVID-19 [49]. This is attributed to hypertension's impact on the cardiovascular system, which can elevate the likelihood of complications such as myocardial injury and ischemia. Furthermore, the severe inflammatory response triggered by COVID-19 may exacerbate hypertension, further elevating the risk of negative outcomes.

Hypertension and COVID-19 share several common risk factors, including advanced age, obesity, and diabetes, which may account for the higher prevalence of hypertension among COVID-19 patients [49]. These shared risk factors can also increase the likelihood of severe illness and death from COVID-19 in individuals with hypertension. Overall, the elevated prevalence of hypertension in COVID-19 patients likely results from a combination of its general prevalence, its association with severe COVID-19 outcomes, and overlapping risk factors.

A systematic review and meta-analysis [48] revealed a strong correlation between age and male gender with severe cases of COVID-19 [50]. Notably, this association was found to be independent of each other. The analysis also identified a positive link between smoking (both current and former) and severe COVID-19. Preexisting CVD, hypertension, and diabetes have been consistently associated with severe COVID-19 across various studies. However, few studies have adequately considered the influence of age and sex on these associations. One study demonstrated that hypertension and diabetes were independently linked to severe COVID-19, even after adjusting for age and other comorbidities [51]. These findings suggest that while age may impact the relationship between hypertension, prior cardiovascular diseases, and severe COVID-19, sex may not exert a similar effect.

Hypertension and IHD are interrelated conditions that exhibit a strong correlation. High blood pressure, a hallmark of hypertension, places excessive strain on blood vessels and the heart, facilitating the formation of blood clots and plaque buildup in the coronary arteries. This increases the likelihood of IHD, characterized by reduced blood flow to the heart muscle, potentially leading to chest pain, heart attacks, and, in severe cases, sudden death. The complex interplay between these conditions is evident in their coexistence and prevalence among COVID-19 patients.

The findings of this review align with previously published research. An umbrella systematic review indicated that individuals with preexisting cardiovascular disease are significantly more likely to experience severe COVID-19, with an odds ratio of 3.86 [52]. This suggests that individuals with cardiovascular diseases are 3.86 times more likely to exhibit severe symptoms compared to those without such conditions [52]. This conclusion was based on a diverse pool of studies, revealing substantial heterogeneity [52]. These results support findings from other published reviews, studies, systematic reviews, and meta-analyses documenting a high incidence of cardiovascular complications in patients with severe COVID-19 infection.

Study limitations and impact

This systematic review acknowledges several limitations that may affect the validity and generalizability of its findings. Most of the included studies were retrospective, which can introduce inaccuracies and potential recall bias in data collection. While we incorporated both interventional and observational studies, the review was restricted to peer-reviewed articles published in English. This limitation may lead to publication bias, as relevant studies not meeting these criteria could offer valuable insights and affect our conclusions. Additionally, during the study selection process, 571 articles could not be retrieved for full-text review, potentially excluding significant research. Furthermore, the majority of included studies focused on hospitalized COVID-19 patients, which may overlook milder cases and limit the applicability of findings to the broader population.

The implications of this review for clinical practice, public health policy, and future research are substantial. Given the focus on hospitalized cases, caution is warranted in generalizing these results to non-hospitalized COVID-19 patients. Our findings indicate that hospitalized COVID-19 patients with cardiovascular diseases are at a higher risk of severe disease. Public health policies should reflect these findings. Future research should not be confined to peer-reviewed journals or English-language articles, as this would help ensure that relevant studies are not overlooked in exploring the relationship between cardiovascular disorders and severe COVID-19.

Conclusion

In summary, this comprehensive review demonstrates a correlation between several cardiovascular diseases—such as hypertension and IHD—and an increased likelihood of severe COVID-19 manifestations and higher mortality rates. Hospitalization for COVID-19 is associated with a potential 25% incidence of cardiovascular complications, highlighting the need for further research to understand the long-term effects of COVID-19 on cardiovascular health. Many cardiovascular risk factors linked to COVID-19 are modifiable, suggesting that enhancing cardiovascular health through targeted prevention strategies may lead to improved outcomes for individuals post-COVID-19.

Declarations

- **Clinical trial number:** Not applicable.
- **Ethics approval and consent to participate:** Not applicable. This systematic review used publicly available data and did not involve direct participation of human subjects.

- **Consent for publication:** Not applicable. As no individual patient data was used, consent for publication is not required.
- **Availability of data and material:** The data used in this systematic review are publicly available and can be accessed through the respective databases (e.g., PubMed, Cochrane Library, etc.). No new datasets were generated for this review.
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- **Competing interests:** The authors declare no competing interests.
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