

Association between cardiovascular disease and severe COVID-19 and mortality rate in COVID-19 Patients: a systematic review and met analysis

Elham Mohammadzadeh¹, Zahra Azadifard², Iman Nosratabadi³, Rahele Alimoradzadeh⁴, Shima Sadat Aghahosseini^{5*}

Corresponding Author: Shima Sadat Aghahosseini^{5}

Corresponder Email : [Email:shima.aghahosseini@sbmu.ac.ir](mailto:shima.aghahosseini@sbmu.ac.ir).

1. MSc in Nursing, Clinical Research Development unit of Razi Hospital, Birjand university of medical sciences, Birjand, Iran. Email: mohammadzadehelham394@gmail.com.
2. Master student of community Health, Lorestan university of medical sciences. Email: zazadifar@yahoo.com
3. Research committee, School of nursing and midwifery, sirjan university of medical sciences, Sirjan, Iran. Email: nosratabadi.iman@yahoo.com.
4. MD, Geriatrician, Firoozabadi clinical Research Development unit, Iran university of medical sciences, Tehran, Iran. Email: Alimoradzadeh.r@iums.ac.ir.
5. *PhD, Assistant Professor, Department of medical surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti university of medical sciences, Tehran, Iran. [Email:shima.aghahosseini@sbmu.ac.ir](mailto:shima.aghahosseini@sbmu.ac.ir).

Abstract

Purpose: evaluate association between cardiovascular disease and severe COVID-19 and mortality rate in COVID-19 Patients.

Method: The present study is a systematic review and meta-analysis (PRISMA guidelines) study based on information collected from regular search of Internet resources using logical functions between keywords in PubMed, Scopus, Science Direct, Embase and scholar uses English keywords between January 2019 and March 2022. 95% confidence interval on odds ratio were done with fixed effect model. Meta-analysis was performed using STATA.V16 software.

Results: the full text of 161 articles was reviewed and finally 15 articles entered the analysis. Odds ratio of association between cardiovascular disease and severe COVID-19 and COVID-19 mortality was 1.05 (OR; 95% confidence interval 0.81 to 1.29; p=0.00) and 0.75 (OR; 95% confidence interval 0.44 to 1.06; p=0.00), respectively.

Conclusion: Meta-analysis shows that patients with cardiovascular disease are directly related to the progression of COVID-19 disease and COVID-19 mortality compared to the control group.

Key words: cardiovascular disease, COVID-19 mortality, COVID-19 disease

Introduction

Coronavirus or COVID-19 has caused many problems in the structure of medical services in various dimensions(1). Because the consequences of the COVID-19 epidemic can be dangerous, especially for people suffering from chronic diseases(2). Therefore, most of the focus of medical centers has been on controlling this disease, so that this issue has neglected to provide services to other patients, including people with cardiovascular problems(3). Given the high risk of COVID-19 disease, it is important to consider how they receive their health services. On the other hand, allocating maximum capacity of medical centers to patients with coronary artery disease may make it difficult to manage other hospitalized patients. Therefore, patients with heart problems face various challenges in receiving services(4, 5). Statistics show an increase in deaths due to heart disease due to delays in receiving medical services compared to before the COVID-19 pandemic(6, 7). Because COVID-19 disease can be very dangerous for these patients. Therefore, the provision of medical services should be done with special consideration. However, the implementation of restrictions in the community to control the disease and receive medical services for cardiovascular patients is associated with problems, and it is necessary for the health care system to make rapid changes in the provision of medical services to heart patients(8). Delays in receiving medical care due to reduced access to outpatient services during a pandemic can increase the severity of illness and mortality. Difficulty distinguishing between the symptoms of coronary heart disease and factors unrelated to cardiovascular disease can lead to mismanagement of the disease, increased rates of injury and death in heart patients(9). Among high-risk patients, heart patients require timely diagnostic tests and screening. Also, people who are candidates for surgery need special equipment and facilities; however, in many hospitals, the lack of equipment has created problems due to the allocation of more resources to patients with Covid-19(10). Recent studies have shown that cases of COVID-19 exposed to baseline cardiovascular disease have a worse prognosis than normal cases, and some cases experience myocardial damage associated with viral infection (11-13). The aim of present study was evaluate the Association between cardiovascular disease and severe COVID-19 and mortality rate in COVID-19 Patients.

Method

Search strategy

Present study is based on PRISMA guidelines(14), all articles published in international databases such as PubMed, Scopus, Science Direct, Embase between January 2019 and March 2022 included; Google Scholar search engine was used. Used PECO strategy to answer the research questions (Table1).

The following keywords were used to search:

((("Cardiovascular System"[Mesh] OR "Cardiovascular Infections"[Mesh] OR "Cardiovascular Abnormalities"[Mesh] OR "Models, Cardiovascular"[Mesh] OR "Cardiovascular Diseases"[Mesh] OR "Heart Disease Risk Factors"[Mesh] OR "Myocardial Infarction"[Mesh] OR "Cardiology"[Mesh]) OR ("Cardiovascular System/adverse effects"[Mesh] OR "Cardiovascular System/classification"[Mesh] OR "Cardiovascular

System/complications"[Mesh] OR "Cardiovascular System/therapy"[Mesh])) AND "COVID-19"[Mesh]) AND ("COVID-19/classification"[Mesh] OR "COVID-19/complications"[Mesh] OR "COVID-19/mortality"[Mesh])) OR ("SARS-CoV-2"[Mesh] OR "SARS-CoV-2 variants" [Supplementary Concept]).

Inclusion criteria

The selection criteria were RCT, cohort and observational studies that articles published in English were selected. Case reports, case-control, reviews and in-vitro studies were excluded.

Table1. PECO strategy

PECO strategy	Description
P	Population: hospitalized COVID-19 cases
E	Exposure: Patients with cardiovascular disease
C	Comparison: Patients without cardiovascular disease
O	Outcome: mortality rate and severe COVID-19

Statistical analysis

95% confidence interval on odds ratio about mortality rate and severe COVID-19 between Patients with cardiovascular disease and without cardiovascular disease were done with fixed effect model and Mantel-Haenszel method. I^2 index test was used to evaluate the level of heterogeneity ($I^2 < 50\%$ = low levels, $50 < I^2 < 75\%$ = moderate and $I^2 > 75\%$ = high levels). Data analysis was performed using STATA.V16 software.

Result

First search for articles in databases, 389 articles were identified. After importing all articles into EndNote.X8 software, duplicate articles were deleted (n=24). 365 article entered and examined in second stage. At this stage, while reviewing the titles and abstracts of articles, 204 unrelated articles were excluded from the study. In the third stage, the full text of 161 articles was reviewed. Finally six articles that were published between January 2019 and March 2022 and met the inclusion criteria, entered the analysis.

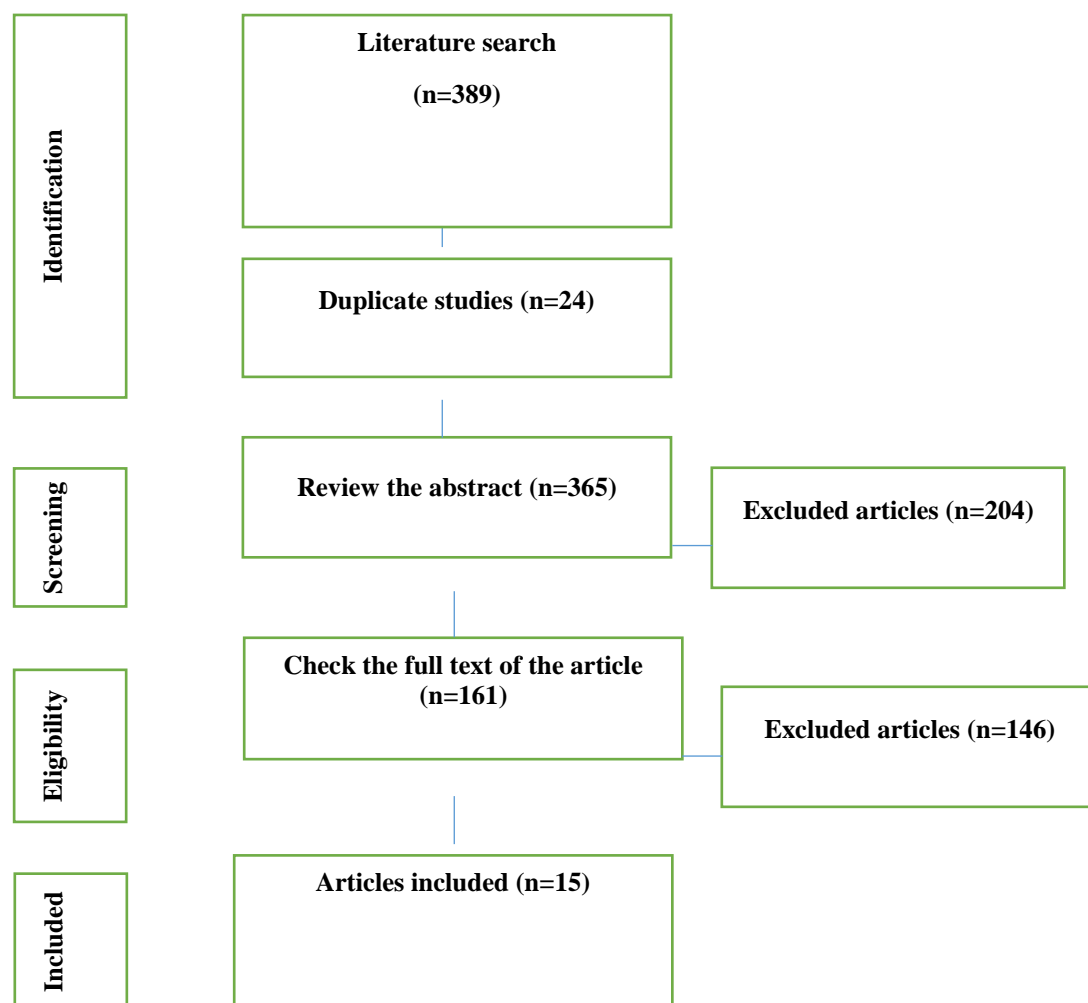


Figure 1. PRISMA flowcharts

Characteristics

All studies that included in present article were Retrospectives observational studies. The number of patients were 5185, 582 Patients were with cardiovascular disease, 299 Severe cardiovascular disease and 286 Non-severe cardiovascular.

Quality of studies

According to NOS tool, all studies had low risk of bias (Table 3).

Table2. Characteristics of studies selected for review in present study

Study. Years	Study design	Number of Patients	Number of Patients with cardiovascular disease	Number of Severe cardiovascular disease patients	Number of Non-severe cardiovascular disease patients
Zhan et al., 2020 (15)	ROs	405	156	77	79

Cocconcelli et al., 2020 (16)	ROs	102	60	25	35
Cen et al., 2020 (17)	ROs	1007	65	34	31
Chen et al., 2020 (18)	ROs	145	1	1	0
Huang et al., 2020 (19)	ROs	202	5	1	4
Li et al., 2020 (20)	ROs	544	34	28	6
Goyal et al., 2020 (21)	ROs	393	54	25	29
Yang et al., 2020 (22)	ROs	200	11	1	10
Wan et al., 2020 (23)	ROs	135	7	6	1
Shu et al., 2020 (24)	ROs	571	12	3	9
Zhang et al., 2020 (25)	ROs	140	12	8	4
Ishii et al., 2020 (26)	ROs	345	23	6	17
Khalil et al., 2020 (27)	ROs	204	24	10	14
Wang et al., 2020 (28)	ROs	59	13	10	3
Xie et al., 2020 (29)	ROs	733	108	64	44

ROs: Retrospective observational study

Cardiovascular disease and severe COVID-19

Odds ratio of association between cardiovascular disease and severe COVID-19 between patients with and without cardiovascular disease was 1.05 (OR; 95% confidence interval 0.81 to 1.29; $p=0.00$) and I^2 was 16.05% with low Heterogeneity ($p=0.29$) (Figure 2). Meta-analysis shows that patients with cardiovascular disease are directly related to the progression of COVID-19 disease compared to the control group ($p=0.00$).

Cardiovascular disease and COVID-19 mortality

Odds ratio of association between cardiovascular disease and COVID-19 mortality between patients with and without cardiovascular disease was 0.75 (OR; 95% confidence interval 0.44 to 1.06; $p=0.00$) and I^2 was 76% with high Heterogeneity ($p=0.00$) (Figure 3). Meta-analysis shows that people with cardiovascular disease have an increased mortality rate compared to the control group ($p=0.00$).

Table3. Risk of bias assessment (NOS tool)

Number of study	Selection (5 score)				Comparability (2 score)	Outcome (2 score)		Total score
	representative sample	Sample size	Non respondents	Ascertainment of the exposure	Based on design and analysis	Assessment of outcome	Statistical test	
Zhan et al., 2020 (15)	1	1	1	1	2	1	1	8
Cocconcelli et al., 2020 (16)	1	1	1	0	2	1	1	7
Cen et al., 2020 (17)	1	1	1	2	2	1	1	9
Chen et al., 2020 (18)	1	1	1	1	1	1	1	7
Huang et al., 2020 (19)	1	1	1	0	2	1	1	7
Li et al., 2020 (20)	1	1	1	2	1	1	1	8
Goyal et al., 2020 (21)	1	1	1	1	2	1	1	8
Yang et al., 2020 (22)	1	1	1	1	1	1	1	7
Wan et al., 2020 (23)	1	1	1	1	2	1	1	8
Shu et al., 2020 (24)	1	1	1	1	1	1	1	7
Zhang et al., 2020 (25)	1	1	1	2	2	1	1	9
Ishii et al., 2020 (26)	1	1	1	1	1	1	1	7
Khalil et al., 2020 (27)	1	1	1	0	2	1	1	7
Wang et al., 2020 (28)	1	1	1	2	1	1	1	8
Xie et al., 2020 (29)	1	1	1	1	2	1	1	8

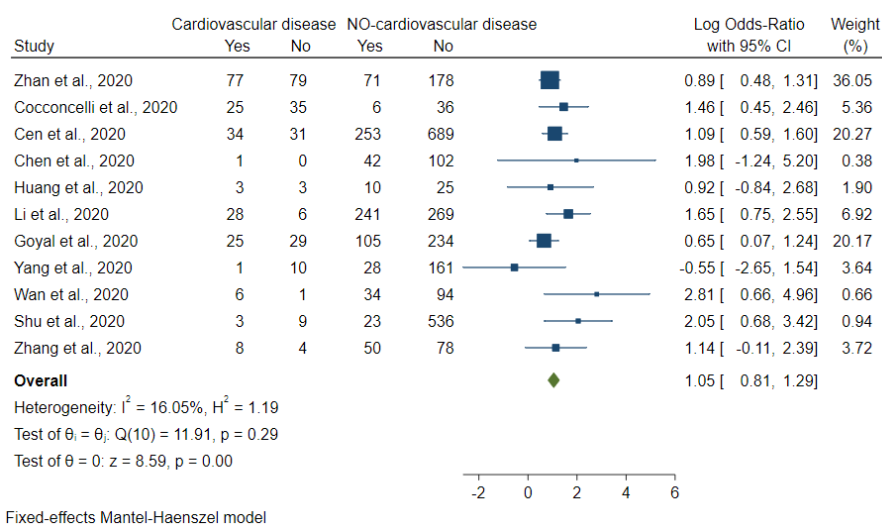


Figure 2. Forest plot showed association between cardiovascular disease and severe COVID-19 between patients with and without cardiovascular disease

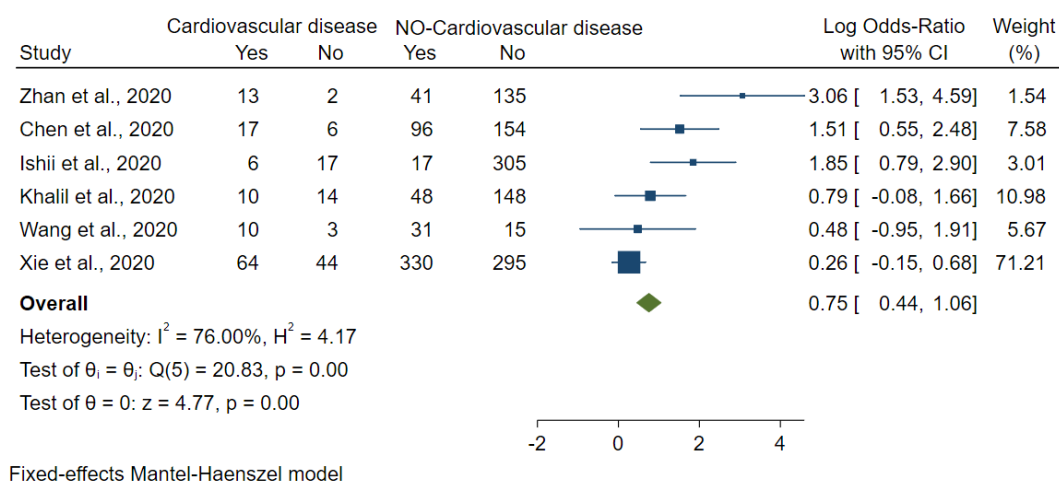


Figure 2. Forest plot showed association between cardiovascular disease and COVID-19 mortality between patients with and without cardiovascular disease

Discussion

A total of 38 million deaths (68%) worldwide are due to non-communicable diseases such as cardiovascular disease, diabetes, chronic respiratory disease and cancer(30). However, during the occurrence of disasters and epidemics of infectious diseases, the problems of cardiovascular patients increase and the management of these patients will face many problems.(31). Based on the findings of the present study, cardiac patients have faced challenges in providing care and surgery, admission and hospitalization since the COVID-19 epidemic, which can be due to lack of resources (physical space, allocation of resources to patients with Covid-19). Restrictions on facilities and equipment (lack of education for patients and medical staff) Fear of infection and lack of sufficient information (Inadequate preparation program) Inadequate planning in service delivery and resource management (Disruption in the quality and quantity of medical services provided (Reduction in the amount of care provided, receiving inappropriate and untimely medical care). Lack of resources is one of the main challenges in the intensive care unit of heart patients.

In the present study, 15 articles that were related to the purpose of the study were reviewed. In the present study, 11% of COVID-19 patients had cardiovascular disease; According to the present meta-analysis findings, a direct correlation was observed between the increase in disease severity and mortality of patients with cardiovascular diseases. Based on the available evidence, most patients with cardiovascular disease show more severe cases of Covid-19; these findings are also related to age (32-34). Patients with cardiovascular disease are at higher risk for acute cardiovascular events, thromboembolism, infection and disease progression after SARS-COV-2 infection(35, 36). The findings of the present study confirm the results of other studies. Previous pandemics such as SARS and MERS have reported similar findings to the present results, so it can be concluded that cardiovascular complications are associated with COVID-19 disease (37-39). On the other hand, studies show that in patients with Covid-19, acute myocardial damage is observed(40). Acute myocardial injury and other cardiovascular diseases are directly related to increased mortality in COVID-19 patients(41, 42). The mechanism of association between SARS-COV-2 and cardiovascular injury is currently

unknown and further studies are needed. Evaluate the treatment of patients with cardiovascular disease, especially during an epidemic that leads to the treatment and prevention of mortality; Side effects of medications should be carefully monitored to prevent exacerbation of the disease. Evidence shows that smokers have an increased risk of cardiovascular disease, resulting in the severity of COVID-19 disease and mortality. The present study had some limitations: first, most studies have been done in China and must be done in other countries for confirmation and evidence; Second, the relationship between age and gender must also be carefully considered; Third, the current smoking status of patients should be examined; Fourth, the heterogeneity between the findings of studies related to mortality and cardiovascular disease was high.

Conclusion

Based on the findings of the present meta-analysis, a direct relationship was observed between the progression of COVID-19 disease and the increase in mortality of COVID-19 patients with cardiovascular diseases. As a result, cardiovascular patients are more at risk of infection and death than others. To confirm the present evidence, studies with higher sample sizes should be performed worldwide.

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