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The association of preexisting cardiovascular risk and the disease severity of COVID-19: A meta-analysis

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Abstract

Background: The exponential growth of novel 2019 Coronavirus disease (COVID-19) has set off a worldwide crisis. Although, its cause mild to moderate illness in major of patients; however, some peoples get critically ill. Peoples with underlying diseases, including cardiovascular complications, diabetics etc. are more susceptible to sever illness. Therefore, it is crucial to understand the association of these severe diseases and COVID-19 is crucial.

Design: This is a meta-analysis of observational studies assessing cardiovascular (CV) complications and the impact of CV comorbidities or risk variables (RF) of hospital-based COVID-19 patients mortality.

Methods: Data sources: PubMed, Scopus, and ISI from 1 December 2019 to 11 June 2020; References of qualified investigations; Abstract of the logical meetings; Cardiology sites. We have chosen to contemplate that report clinical results of patients with COVID-19 in the medical clinic. The principal result was death. Auxiliary results were CV side effects and CV functions observed during the COVID-19-related clinic. The separated information was recorded in Excel worksheets and investigated utilizing measurable programming (MedCalc, Open Meta-analyst R). We used a 95% CI level as a brief measure.

Results: As a result of 17 studies, 11% of the 54565 patients hospitalized had CV complications or CV related RF. Clinical and vascular complications were noted in 16.91% of cases during the observational period. In a meta-relapse study, cardiovascular disease (CVD) or RF was mainly associated with CVD in COVID-19 patients ($p = 0.020$). The occurrence of previous CVD or RF ($p < 0.001$), mature age ($p < 0.001$), and the advancement of cardiovascular intricacies when hospitalized ($p = 0.040$) was statistically significant.

Conclusions: CVD are elementary in COVID-19 patients, and alongside previous CV comorbidities and RF can prompt unfavorable clinical functions and mortality. Physician far and wide ought to know about this relationship to recognize patients at higher risk.

1. Introduction

The novel 2019 Coronavirus disease (COVID-19) is a serious health issue around the globe and effect almost every age of peoples in a various way. As of Nov 05, 2020 more, than 50 million cases are reported around the globe with more than 1 million deaths. This illness has demonstrated a heterogeneous clinical profile, varying from the asymptomatic carrier state to the deadly result of multi-organ failure and a wide range of case fatality rates varying from 0.5 to 65%. (Bansal, 2020; Lai et al., 2020). Nonetheless, the risk factors for COVID-19 severity are still not known. The available data is significant for distinguishing high-risk patients and advancing readiness (for instance, surveying the requirement for clinic beds and mechanical ventilators) (Ou et al., 2020; Wolff, Nee, Hickey, & Marschollek, 2020). These risk factors additionally have consequences for labor force reallocation (eg, movement of medical services laborers with explicit risk elements to working environments with a diminished risk of presentation to COVID-19). By and large, the new COVID-19 caused the moderate infection, however, can cause extreme pneumonia in certain patients and lethal in others (Jiang et al., 2020; Koh, Shah, Chua, Gui, & Pang, 2020; Yong Sun et al., 2020).

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The current meta-analysis focused on the association of preexisting CV risk and the disease severity of COVID-19 hospitalized patents. Furthermore, we also investigate the effect of CVD on the mortality rate of COVID-19 hospitalized patents. The study will provide an overview for the physician and health care provider to assess the risk of CVD in COVID-19 hospitalized patients, which may be helpful for management for such patients in clinical settings.

2. Literature review

More established individuals and individuals with previous clinical issues, (for example, lung infection, constant respiratory sickness, or diabetes) are at risk of severe illness(Ejaz et al., 2020). While the respiratory tract is the most frequently implicated organ system in this disease, other organs, and especially the heart, are also affected with a negative effect on the outcome of the disease (Zheng, Ma, Zhang, & Xie, 2020). In addition, pre-existing cardiovascular disease (CVD) may influence the incidence and mortality of these patients. Despite countless reports of CVD in COVID-19 patients, there are still a host of unresolved questions.

In any case, it is significant for the physician to get CV patients to think about the clinical setting, regular history, and risk factors for COVID-19 contamination. SARS-CoV-2 is believed to infect host cells via ACE2 to trigger COVID-19, thereby causing myocardial damage, even though exact mechanisms are unknown. Patients with potential CVD and SARS-CoV-2 contamination have an adverse outcome. Particular consideration should also be paid to cardiovascular safety while treatment with COVID-19 (Clerkin et al., 2020; Huang, Xie, Chen, Hong, & Huang, 2020).

3. Methods

3.1 Studies selection

We included those clinical studies which reported CVD or CV RF in COVID-19 patients. Those studies which are duplicated or where CVD or CV RF are not clearly identified were excluded. From December 1, 2019, to August 30, 2020, we reviewed the PubMed, Scopus, and Google Scholar and used the keywords: cardiovascular, COVID-19, cardiovascular diseases. The following sentences are used: I) PubMed MEDLINE - (("COVID-19" [Fields] Coronavirus 2 severe respiratory disorders in ORA "2019" [all fields]) cCoV2 in ORA [all fields]) AND (("Cardiovascular Framework" [MeSH Conditions] ORA ("Heart-Vein" "[Arils Areas] O" Heart-Veins "[Fields Fields]) ORA (" Heart-Veins "[MeSH Conditions] O "Heart" Fields Fields] ORA ("Blood vessels" [MeSH conditions] ORA ("Blood" [Fields Fields] and "Veins"; ii) SCOPUS - SARS-COV-2 Cardiovascular in Coronavirus ORA VE; iii) ISI Web of Science COVID-19, Cardiovascular Disease. The issues for the self-selection of two constructive (JS, plus SDR) examinations reviewed the knowledge base. No debate emerged.

Chinese examinations that outcome legitimately from the information base pursuit are converted into English before being checked. Non-English references have been overlooked. Preprinted compositions were expected to help the utilization of the majority of the accessible examinations. The study of disease transmission and network announcing from out-of-medical clinic patients, just as situations where no clinic passing is accounted Without proof, the corresponding authors were reached employing email to demand additional data. Table 1 summarized the detailed exclusion and inclusion criteria based on PICOS.

3.2 Inclusion Criteria:

Those clinical studies were included which reported CVD or CV RF in COVID-19 patients. The study incorporates review considers, contextual analyses, and examination letters announcing: clinic patients with COVID-19 and medical clinic results with cardiovascular comorbidities and detailed risk factors.

3.3 Exclusion Criteria:

Those studies detailing information that has just been distributed in another examination (if there should arise an occurrence of duplication, the biggest investigation announcing the necessary information will be chosen). Time or spot of affirmation is not depicted. The study of disease transmission and network announcing from out-of-medical clinic patients, just as situations where no clinical examination was mentioned.

3.4 Data extraction and quality assessment

Three researchers independently removed information on research qualities and recurrence of frequency from included articles. We freely estimated the consistency of each study. The assessment was done in the exploration stage and depended on the principle aftereffects of the investigation (CV comorbidities and/or difficulties of patients with Covid-19). The conflicting factors have been brilliantly resolved. We used the afterwards mention data: quality of patients; Ages; Gender; geographical area, CV risk during the census; previous CVD history; Hospitals (transient,

cardiovascular death, AMI, myocardial injury, stroke, cardiovascular disorders). The risk factors for COVID-19 severity were assessed independently. Duplicated studies were carefully evaluated and removed where required. In the case of two similar studies, we choose the study with a large number of population. By and large, the new 2019 (COVID-19) caused a moderate infection, however, can cause extreme pneumonia in certain patients and lethal in others.

3.5 Data analysis

Our main findings are based on evidence of CVD and/or complications in patients with COVID-19, and utilized CI 95%. We used Freeman-man turkey test as described previously [10] to measure the weighted summary proportion under the random-effects model. Heterogeneity was checked using the Cochrane Q test using quadratic power. Scores below 0.10 were representative of homogeneity. We used I^2 scores to evaluate the difference between concentrates because of heterogeneity. Affectability were acted within the sight of heterogeneity to decide the conceivable effect on execution. We used Arcsine of square root proportion (ASRP) as the metric when a group had zero events with correction for continuity for subgroup meta-analysis, as mentioned previously(De Rosa et al., 2018). A meta-regression study was used to examined CVD, or CV RF and CV related deaths. An endeavor was made to apportion the channel utilizing channel graphs. Areas were directed utilizing MedCalc 15.8 and Open Meta-Analytics and R (The R Foundation).

4. Results

4.1 Study characterization

As shown in Figure 1, we explored 1,897 records from 17 qualified examinations announcing clinical results for hospitalized patients positive for SARS-CoV-2 infection (Table 1). To evade the reiteration of results, all studies were checked for examination comparable to the area and period contribution.

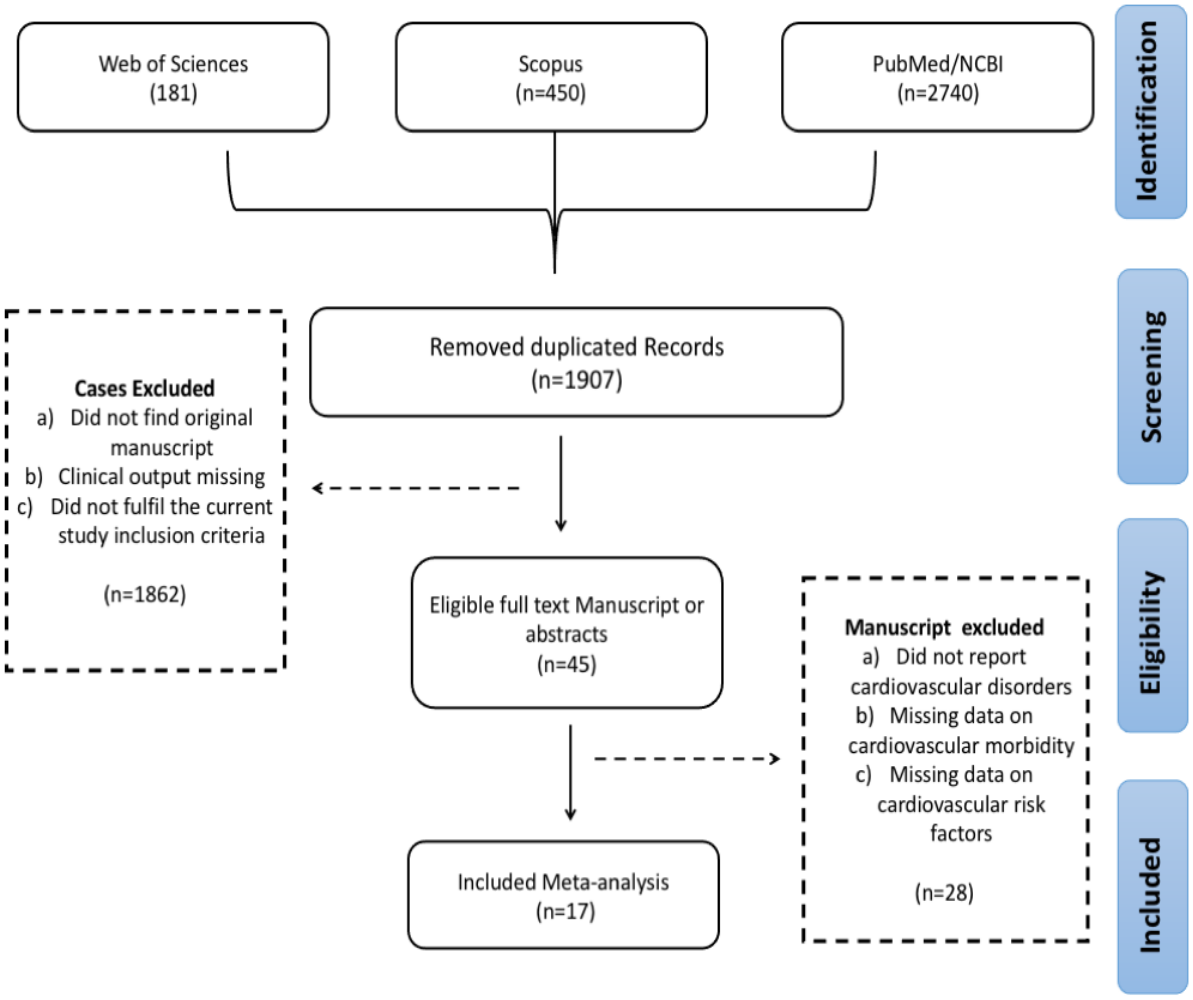

Figure 1. **Study search and selection and selection criteria based on the PRISMA flow chart.**

The studies included emergency clinic patients from various geographic areas, including Asia, Europe, and the United States. Altogether, clinical results of 54565 hospitalized COVID-19 patients were recorded in the current study (Table 2). The mean quality order of the included examinations was evaluated as "fair" as indicated by the NIH quality appraisal for review and Cross-Sectional Studies of the NIH (Table S1). The studies express their objective. The objective was characterized in 20 studies with less exact measures for support in just one of the included studies. The enrollment pace of qualified patients was extremely high in all studies. Generally speaking, the exhibition estimations were very much characterized. Specifically, the outcomes were clearly defined.

Table 1. **Major characteristics of the study**

	Number of participants	Male	Female	Average Age	Center/Hospital/ Institute	Recruitment time	Reference study/Organization
1	1591		287	63	Italy—ICU Network Lombardy	20/02/20–18/03/20	Grasselli G(Grasselli et al., 2020)
2	41		11	49	China—Wuhan (Jin Yin-tan Hospital)	16/12/19–02/01/20	Huang C(C. Huang et al., 2020)
3	52		17	59.7	China—Wuhan (Jin Yin-tan hospital)	24/12/19–26/01/20	Yang X(Yang et al., 2020)
4	393		155	62.2	U.S.—NY Presbiterian + New York Cornell (2 Hospitals)	03 March, 2020–27 March, 2020.	Goyal P(Goyal et al., 2020)
5	49		18	43.6	China—Wuhan (Fifth Medical Center of Chinese PLA General Hospital)	20 Jan, 2020–16 Feb, 2020.	Ji D(Ji et al., 2020)
6	1099		459	47	China—Medical Treatment Expert Group for Covid-19 (552 Hospitals in 30 provinces)	11 Dec, 2020–29 Jan, 2020.	Guan W(Guan et al., 2020)
7	54		25	42	Singapore—National Center for Infectious Diseases	26 Jan, 2020–16 Feb, 2020.	Sun Y(Y. Sun et al., 2020)
8	44672		21691	45.9	China CDC	31 Dec, 2019–11 Feb, 2020.	China CDC(Novel, 2020)
9	5700		2263	63	U.S.—NYC + Long Island + Werchester C (12 Hospitals)	01 March, 2020– 04 April, 2020.	Richardson S(Richardson et al., 2020)
10	180			82	U.S.	01 March, 2020–30 March, 2020.	Garg S(Garg et al., 2020)
11	137		76	57	China—Wuhan, Xiaogan, Yichang, Jingzou, Enshi Tujia and Miao, Shiyan	30 Dec, 2019–24 Jan, 2020.	Liu K (Liu et al., 2020)
12	99		32	55.5	China—Wuhan (Jin Yin-tan Hospital)	01 Jan, 2020–20 Jan, 2020.	Chen N(Chen et al., 2020)
13	28		13	42.6	Korea—National Committee	19 Jan, 2020–17 Feb, 2020.	Kim ES(Kim et al., 2020)
14	80		38	44	China—Chongqing	Jan-2020—Feb 2020	Wu J(Wu et al., 2020)
15	138		63	56	China—Wuhan (Zhongnan Hospital)	01 Jan, 2020–28 Jan, 2020.	Wang D(Wang et al., 2020)
16	112		59	62	China—Wuhan Union Medical Center	20 Jan, 2020–15 Feb, 2020.	Peng YD(Peng et al., 2020)
17	140		69	57	China—Wuhan (Number 7 Hospital)	16 Jan, 2020–03 Feb, 2020.	Zhang JJ(Zhang et al., 2020)

4.2 Cardiovascular risk profile of hospitalized COVID-19 patients

A total of 39.09% (95% CI = 34.31-39.23) of the registered patients (n = 54565) were women (Figure 2). The average age was 47.2 ± 19.7 years. Among the included patients, 11.03% (95% CI = 7.13–15.02) showed a significant difference between some cardiovascular patients, and exhibit significant amount of heterogeneity among the studies (I^2 = 99.7%; Q = 1511; p <0.001) (Figure 2). Surprisingly,

34.24% of patients (95% CI = 19.54-45.43) were suffering from high pressure (Figure 2). In the study, 17.68% (CI = 10.12-22.32) of patients have diabetes (Figure 2). 09.98% of patients (95% CI = 4.98–16.48) smoked. 29.08% of patients with a clinical history of Obesity (95% CI = 25.46-29.19). We found in 9.09% of patients of coronary heart disease (CHD) (95% CI = 6.76–12.93). Heart failure was found in 11.04% of patients with a clinical history (95% CI = 7.28-09.98).

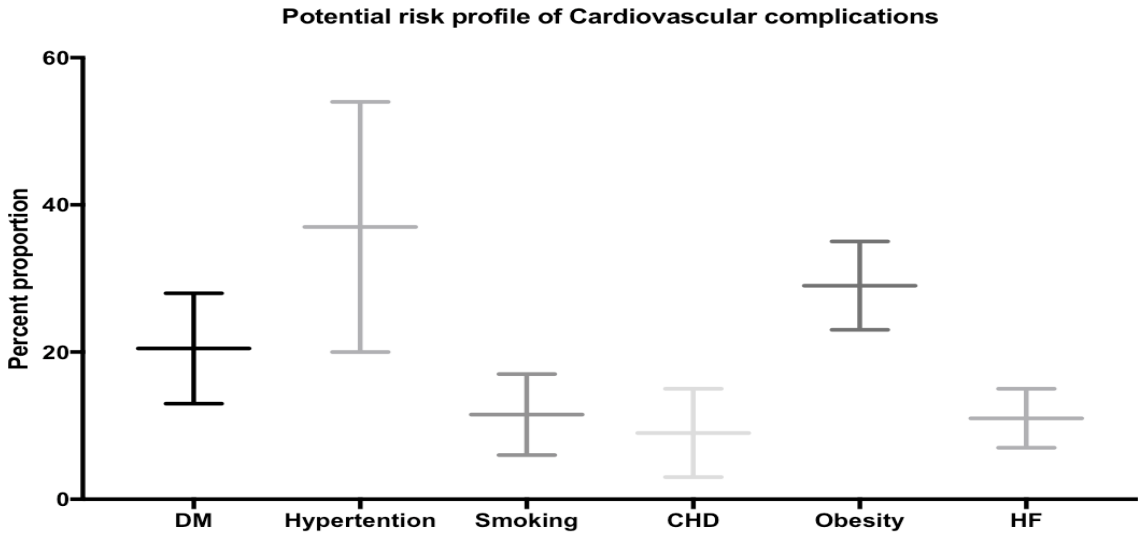

Figure 2. **Cardiovascular risk profile in COVID-19 positive patients. DM; Diabetes mellitus, CHD; coronary heart disease, HF; Heart Failure.**

4.3 Cardiovascular complications in hospitalized COVID-19 patients.

Cardiovascular risk was 16.91% (95% CI = 10.26-20.23) (Figure 3). 09.98% of patients (95% CI = 6.73-14.62) had heart muscle injury (myocardial injury). 09.95% of patients had angina (95% CI = 4.27-19.21). The rate of arrhythmias or palpitations was 19.22% in patients (95% CI = 8.34–29.14). Acute heart failure and myocardial infraction were 2.01% (95% CI = 1.01–2.04) and 2.98% (95%CI = 3.25–6.43), respectively. The mortality rate was 9.6% (ASRP = 0.19; 95% CI = 0.15-0.31), which was not high among these result (I2 = 99.6%; Qp <0.001). A more deep analysis found that mortality in ICU and non-ICU patients were 39.7% (ASRP = 0.51; 95% CI = 0.31–0.78) and 8.1% (ASRP = 0.06; 95% CI = 0.02–0.21), respectively.

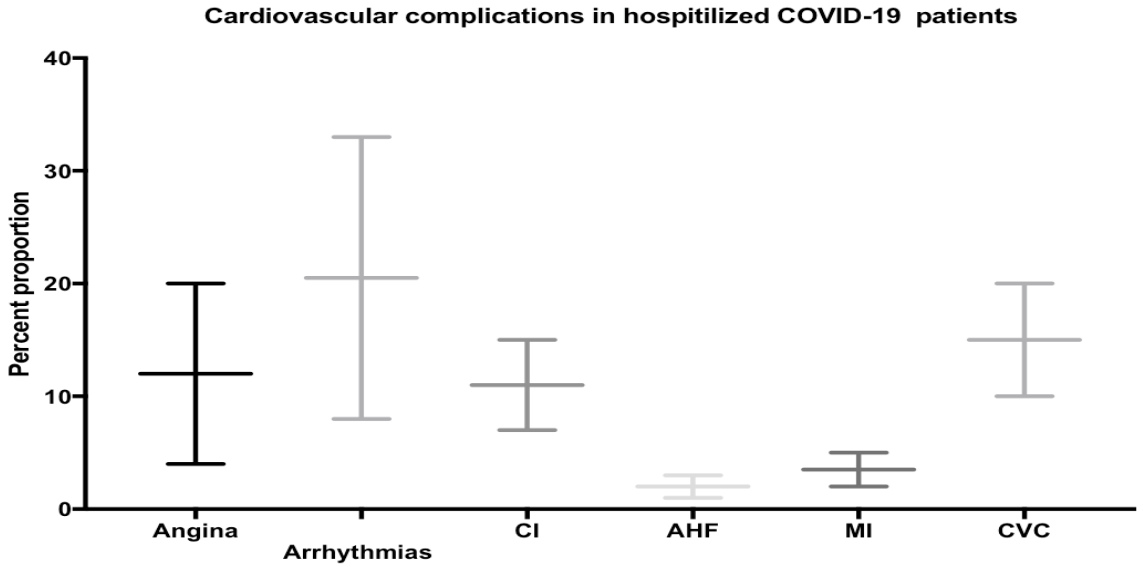

Figure 3. **Cardiovascular complications in COVID-19 positive patients. CI; Cardiac injury, AHF; Acute heart failure, MI; Myocardial infraction, CVC; Cardiovascular complications.**

4.4 CV complications and case fatality at meta-regression analysis.

A history of CVD or CV RF are significant predictors factor of CV complications suffering from COVID-19 (p = 0.024). Our result found that gender (p = 0.19) and age (p = 0.096) were not significantly correlated. However, CV RF (p<0.001) and age (p<0.001) in the CVD during COVID-19 (p = 0.040) significantly correlated with mortality (Table 2).

Table 2. **CV complications and case fatality at meta-regression analysis.**

Predictors	Factors	95% CI	P-value	Regression coefficient
Case fatality	Age	-0.003-0.008	p<0.001	0.006
	Cardiovascular risk factors	0.003-0.005	p<0.001	0.004
	Cardiovascular disorders	0.0-0.003	p=0.040	0.001
Cardiovascular complications	Age	-0.005-0.026	p=0.20	0.001
	Sex	-0.024-0.005	p=0.18	-0.011
	Cardiovascular risk factors	0.001-0.009	p=0.02	0.005

5. Discussion

The study examined the incidence of coronary heart disease and complications in COCID-19 hospitalized patients. This meta-study found that a significant proportion (14.1%) of hospitalized COVID-19 patients had CV problems or complications. Overall, the mortality rate was 9.6%. Of course, ICU patients have the highest mortality rates, many times higher than individuals who are not admitted in ICU. CVD is a common outcome in various viral infections and leads to mild to severe myocardial complications (Fong, 2009).

In a multi-center survey GAO et al. (Gao et al., 2020) reported the incidence of heart disease in clinical patients infected with avian influenza A (H7N9) virus (63.2%). The results of the study found that when the H1N1 pandemic took place in 2009, about 54% of those affected had a heart attack. Ludwig et al. demonstrated that between 2010-2012 cardiac patients who used medication of cardiac biomarkers diagnosed with viral infection showed a high level of TNI and/ or CK-MB in 24% of total patients (Ludwig, Lucero-Obusan, Schirmer, Winston, & Holodniy, 2015). Several reports have theorized the potential for a direct public attack that could lead to heart disease related to the disease (de Jong et al., 2006). Whereas, in numerous infections caused by virus can trigger the immune system and lead of cytokines release storm and injure the cardiac muscle (Hochstadt, Meroz, & Landesberg, 2011). Based on the finding of previous studies, the 10.34% myocardial injury rate is in good agreement with the previous studies. CVD or CV RF is responsible for increase death ration in COVID-19 hospitalized patients. Which was also supported by numerous clinical studies conducted across the globe (Ferrari, Di Pasquale, & Rapezzi, 2020; Srivastava, 2020). Previous studies documented that severe CVD patients have a high mortality rate among COVID-19 infected individuals.

On the other hand, hypersensitivity to different inflammatory diseases can lead to an exaggerated, inconspicuous response to the advent of cytokines and abnormalities in the heart muscle. Like COVID-19 pandemic, in other viral pandemic such as influenza, the CV related complication were higher and reported high death ratios. Indeed, data from the severe H1N1 pandemic in 2009 showed that elevated TNI and left ventricular systolic dysfunction (EF<50%) were associated with high mortality (Chacko et al., 2012). Pearce et al. (Pearce, McCaw, McVernon, & Mathews, 2017) previously reported that a subtype of influenza virus which affect the respiratory track and induce CV complications. Their study verifies that respiratory track virus is associated with the CV complications.

It will well established that COVID-19 mainly affect the respiratory tract, our study demonstrated that CVD or CV RF are directly related to the increased CV complications and mortality rate in COVID-19 patients. Our study provides suggestions for further investigations of the underlying mechanism, incidences and CV manifestations in COVID-19 patients. Furthermore, a more deep insight into individual CV RF and its association with COVID-19 patients is vital. Which will help the clinician and health care providers to manage the COVID-19 patients based on their underlying others complications, and will be helpful for reduced the mortality COVID-19 patients who are already suffering from other complications.

Our study is consistent with the subsequent impact of a report (Matsushita et al., 2020) that diabetes and CVD are free indicators of a more severe pathway for COVID-19. Our study bases and extends these findings and shows that CV risk

variability and CVD are free indicators of CV complications caused by infection and death.

6. Implications

The current meta-analysis will be helpful for clinicians and health care providers to strengthen their knowledge for the management of COVID-19 positive patient who is already suffering from CVD or CV RF.

7. Limitation

The current meta-analysis has several limitations. The data recorded in the included examinations were gathered as far as an episode that affected the wellbeing framework. There may likewise be fractional reports that could be considered concerning the circumstance. The included studies didn't follow similar standards for deciding helpful endpoints. Specifically, different biomarkers were utilized during the investigations to group CV complication.

8. Conclusions and future perspective

To sum up, the finding of the current study revealed that CVD or CV RF could significantly increase the mortality rate in COVID-19 patients. Furthermore, this study highlights numerous prognostic factors that are required to consider for further in-depth investigation. The underlying mechanism of various factor needs to be further investigated, which will be beneficial for the physician to aware of the potential risk of CVD and CV complications with the COVID-19 patients.

Conflict of interest

All the author declare that they have no conflict of interest to declare.

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None

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