

Acute Cardiac Injury and COVID-19 – A Systematic Review and Meta-analysis

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Abstract

Introduction:

The ongoing global pandemic, coronavirus disease 2019 (COVID-19), an illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has ranged from an asymptomatic state to unprecedented number of deaths worldwide. In symptomatic patients, a viral pneumonia can unrelentingly progress to multi-system failure with preferential cardiac tropism. Although the full spectrum of COVID-19 cardiac manifestations is still not clear; acute cardiac injury (ACI) remains a common finding. The goal of our study, not only is to examine the current prevalence of ACI among COVID-19 infected patients but also, the reported mortality.

Method:

After thoroughly searching the literature for appropriate studies, a systematic review and meta-analysis were performed. Inclusion criteria were 1) Cohort study, case-control study, or case series study. 2) The study population included individuals with COVID-19 3) The presence or absence of cardiac injury was reported in the study 4) Mortality among patients with cardiac injury is reported or can be calculated.

Results:

Ten studies were included with a total of 1664 patients. The prevalence of ACI was 30.8%. The mortality rate among patients with concurrent COVID-19 and ACI was 53%.

Conclusion:

ACI can occur in one third of patients with COVID-19. Concurrent COVID-19 and ACI entails a high mortality rate. Serum troponin level can be a good prognostic tool in COVID-19.

Introduction

Coronavirus disease 2019 (COVID-19), also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is an ongoing pandemic that not only has challenged our understanding of viral pathogens but also our ability to identify and treat infected patients. Although infection rates continue to fluctuate; reported mortality rates have range between 3.6% and 5.7%.¹

The bewildered infectious disease experts and the rest of the medical community continue to see COVID-19 cases ranging from asymptomatic/mild upper respiratory tract symptoms to severe illness, now believed to be triggered by a hyperinflammatory response cascade affecting many organs leading to death.²

Even though acute cardiac injury (ACI), a well known complication of viral illness, affecting up to 25% of adult patients with influenza;³ there is paucity of data regarding ACI among COVID-19 infected patients.

Consequently, our aim was directed to investigate the prevalence and mortality risk among patients with concurrent COVID-19 and ACI.

Method

PubMed, Google Scholar, ResearchGate, and Google were searched for studies that reported cardiac injury in patients admitted with COVID-19 infection. Inclusion criteria were: 1) Cohort study, case-control study, or case series study. 2) The study population included individuals with a confirmed COVID-19 infection 3) The presence or absence of cardiac injury, which was defined as an elevated level of troponin > 99th percentile with or without other cardiac manifestations, was reported in the study. 4) Mortality among patients with cardiac injury is reported or can be calculated and compared to patients with COVID-19 but no cardiac injury.

A total of ten studies met our inclusion criteria. We had two groups in our meta-analysis. The first group was patients with COVID-19 and ACI and the second group was patients with COVID-19 and no cardiac injury. Pooled analysis was performed using the Review Manager 5.4 software. A random effect model was utilized. The risk ratio between the two groups was reported with its 95% confidence interval (95% CI). The chi-squared statistic, its degrees of freedom (df), and the I^2 index were used as measures of heterogeneity.

Results

A total of 99 studies were initially identified. After careful assessment, ten studies with a total of 1664 patients were appropriate for inclusion in our study. All of these studies were retrospective observational studies.

In our analysis, ACI was prevalent in 30.8% of the hospitalized patients (513/1664). Of the 513 patients with cardiac injury, 272 patients, resulting in a mortality rate of 53% among patients with concurrent COVID-19 and cardiac injury.

Of note, the mortality rate among COVID-19 patients without documented cardiac injury was 14.7% (170/1151).

Risk ratio was 3.41 (95% CI [2.33,4.98]), a statistically higher risk for death among the first group. I^2 index was 81%. (*Figure 1.*)

Discussion

In our pooled analysis, almost one third of COVID-19 infected patients had ACI with a mortality rate of 53%. Although the exact mechanism by which COVID-19 causes ACI remain poorly understood. Potential mechanisms currently proposed either invoke a direct damage to myocytes as a result of systemic inflammation, myocardial interstitial fibrosis, interferon mediated immune response, exaggerated

cytokine response by Type 1 and 2 helper T cells or the secondary effect of coronary plaque destabilization as well as the profound hypoxia these patients have as a result of the overwhelming pneumonia.⁴

Furthermore, Zhou et⁵ al have also demonstrated the relationship existing between COVID-19 and angiotensin-converting enzyme 2 (ACE2), which is a monocarboxypeptidase renin-angiotensin-aldosterone system enzyme that metabolizes several peptides, to enter ACE2-expressing cells. ACE2 is widely expressed in the endothelium of the heart and kidneys,⁶ and that might explain the prevalence of ACI and acute kidney injury among patients with COVID-19. Additionally, ACE2 generates angiotensin 1-7, which decreases myocardial levels of pro-inflammatory cytokines (i.e., TNF α and IL-6).⁷ One of the proposed mechanisms for ACI in COVID-19 is downregulation of ACE2 expression with subsequent accumulation of pro-inflammatory cytokines in the myocardium; however, the effect of COVID-19 on ACE2 serum level, tissue expression, and function is still not clear. Furthermore, COVID-19 is associated with a hypercoagulability state due to an increase in the procoagulant factors, such as fibrinogen.^{8,9} This hypercoagulability state may result in microthrombi formation, which precipitates ACI.

Regardless of the underlying mechanism, ACI was associated with a significantly higher mortality rate. More data is urgently required to better understand the apparent complex tropism that appears to link COVID-19 with ACI not only to identify patients at risk but also provide effective treatment options.

Limitations:

Aside from this being a retrospective study and that most studies were done on Chinese population, which makes generalizability another limitation; it is also important to recognize the relatively high heterogeneity as indicated by an I^2 index value of 81%. Notwithstanding we cannot discard that fact even though this strain of SARS-CoV 2 has shown an increased propensity for developing extra-pulmonary complications, namely ACI, its reported involvement is most likely underestimated. First, initial focus from the outset of the pandemic was simply given to the more common respiratory symptoms. Second, cardiac involvement such myocarditis could have occurred and since in most cases is often self-limiting, would not have recorded. Third, there has been a large number of deaths occurring outside the hospital setting of patients that either decided to stay home or of individuals at other institutions, such as Nursing Homes, where the cause of death would never be known. Last, some case reports have reported patients presenting for other reasons, that were later found to be COVID-19 positive whose cardiac enzymes were probably never assessed and could have had subclinical manifestations.

Conclusion

Based on our results, ACI is common among hospitalized patients with COVID-19 and can be seen in up to one third of these patients and correlates with a higher level of mortality. Serum troponin level should be checked in all patients with COVID-19 for its prognostic value.

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Figures

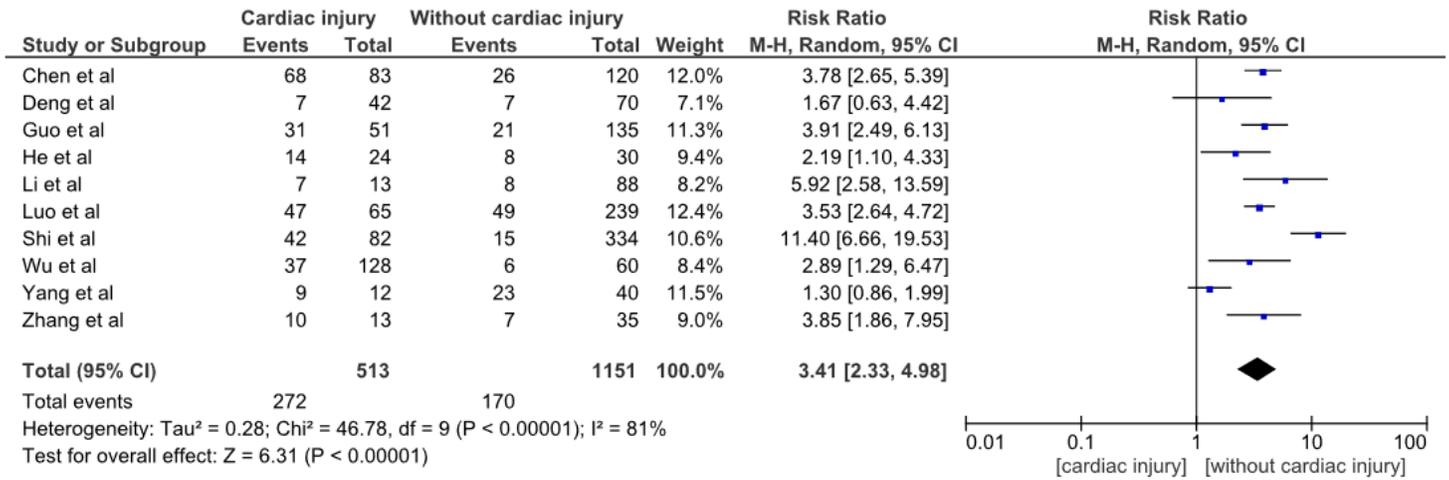


Figure 1

A forest plot of the pooled data analysis.