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# Hellenic Journal of Cardiology

journal homepage: <http://www.journals.elsevier.com/hellenic-journal-of-cardiology/>



## Research Correspondence

# Coronavirus-2019 status on admission increases in-hospital mortality of acute coronary syndromes: A systematic review and meta-analysis



### Keywords:

Acute coronary syndromes  
coronavirus-2019  
mortality  
primary percutaneous interventions  
acute heart failure  
thrombosis

During the recent coronavirus-19 (COVID-19) pandemic, 4.0–9.0% of patients admitted with acute coronary syndromes (ACS) had concurrent positive COVID-19 test result.<sup>1,2</sup> To further examine their in-hospital course, we searched (by keywords shown in Fig. 1) the *PubMed* and *Google Scholar* databases for relevant studies, available throughout December 2021; the references of pertinent articles were manually checked for potential additional inclusions. Eligible papers consisted of observational studies and registries, reporting on in-hospital mortality of patients with ACS, in reference to COVID-19 status on admission. We excluded animal studies, systematic reviews, meta-analyses, case reports, and editorials. The methodology adhered to current guides,<sup>3</sup> with the analysis aided by the *RevMan5* software.<sup>4</sup>

We screened 1204 records and eventually included 17 studies in our meta-analysis. Fever was recorded in 13.4% of COVID-positive ACS patients, but severe respiratory infection or acquired respiratory distress syndrome was absent. Interestingly, the incidence of dyslipidemia (odds ratio 0.87,  $p = 0.02$ ) and smoking (0.72,  $p < 0.001$ ) was less common among COVID-positive ACS patients, but hypertension (1.38,  $p < 0.001$ ) and diabetes (1.51,  $p < 0.001$ ) were more common. Although the incidence of ST-elevation myocardial infarction was comparable (odds ratio 0.96,  $p = 0.65$ ), COVID-positive ACS patients had poorer left ventricular function on admission and were twice as likely to present with dyspnea.

Of the total cohort of 19572 patients, in-hospital mortality was 9.5%. The  $\chi^2$  and  $I^2$  tests indicated a low level of heterogeneity among studies (Fig. 2). There were 1382 (7.6%) deaths among the 18143 ACS patients tested negative for COVID-19; by contrast, there were 482 (33.7%) deaths among the 1429 COVID-positive ACS patients. The (fixed effects) Cochran–Mantel–Haenszel approach<sup>5</sup> revealed a highly significant ( $p < 0.001$ ) mortality difference, with a risk ratio of 5.34 (95% confidence intervals 4.84–5.90) in COVID-positive ACS patients.

The explanation for this markedly increased in-hospital mortality of COVID-positive ACS patients is likely multifaceted, but two points deserve particular attention: *First*, hypertension and diabetes were more common in these patients, in keeping with reports suggesting that these risk factors are shared by both entities.<sup>6</sup> *Second*, COVID-positive ACS patients had increased angiographic thrombus burden, such as multi-vessel thrombosis and higher thrombus grade. Microvascular obstruction post-PCI<sup>7</sup> and cardiogenic shock<sup>1,2</sup> were also more common, coupled with an alarming four-fold higher rate of (acute or subacute) stent thrombosis.<sup>2</sup> These observations are in line with endothelial dysfunction<sup>8</sup> and prothrombotic milieu<sup>9</sup> accompanying the release of pro-inflammatory cytokines along the course of COVID-19 infection.

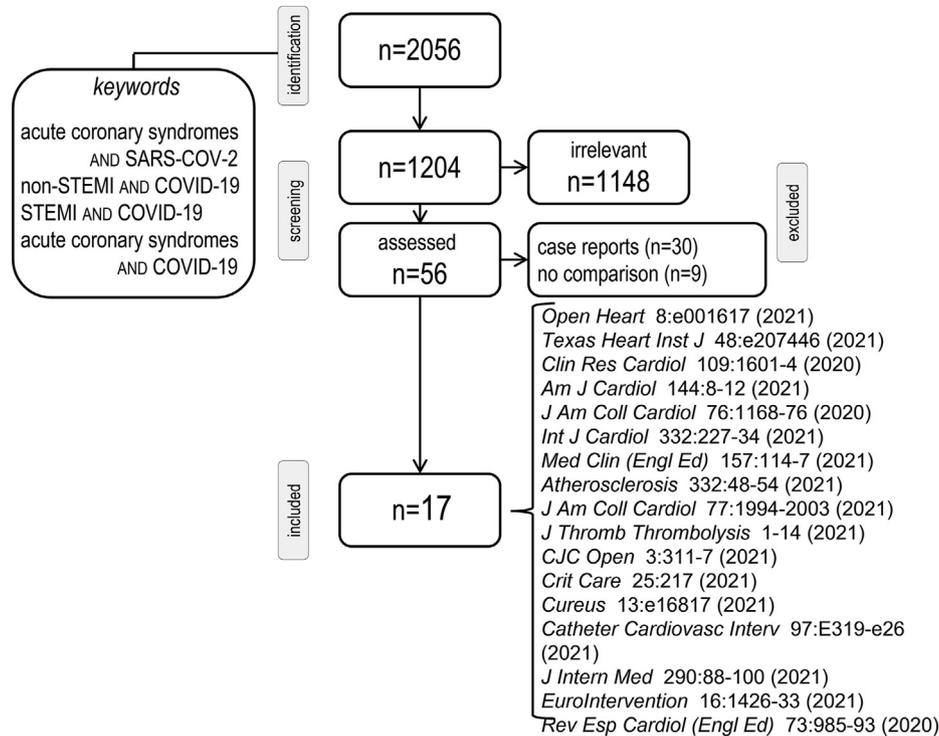
Treatment approaches for COVID-positive ACS patients may have deviated from current guides during the pandemic, especially during the early phase, reflecting variations in the availability of cardiac catheterization services and local epidemiologic conditions. For example, such patients were less likely to undergo primary PCI in the UK, as shown by rates of 30.2% versus 53.9%, reported in a nationwide database.<sup>1</sup> However, the impact of adopting more conservative practices remains uncertain, given the higher thrombotic complications post-PCI in COVID-positive ACS patients.

Our study demonstrates that patients admitted with ACS and concomitant positive COVID-19 have more comorbidities, and their in-hospital course is often complicated by thrombosis. Despite the five-fold increase in mortality, optimal reperfusion and anticoagulation strategies remain unclear.

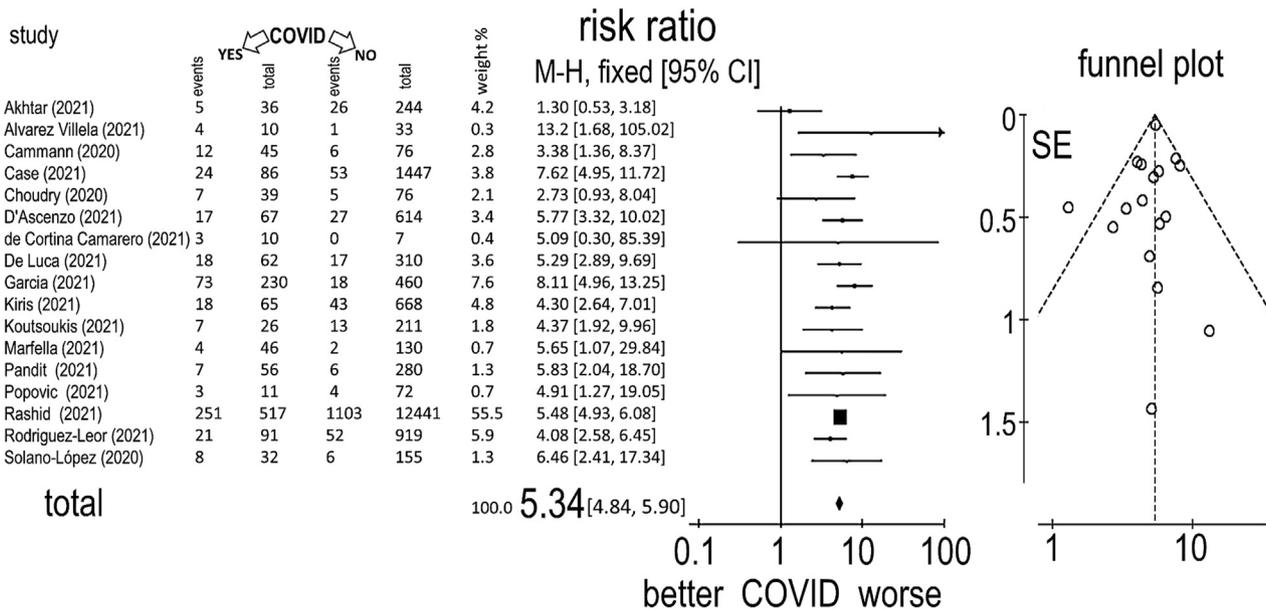
Peer review under responsibility of Hellenic Society of Cardiology.

<https://doi.org/10.1016/j.hjc.2022.06.001>

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**Figure 1.** PRISMA flow diagram. After the screening of 1204 studies (keywords shown on the left), 17 were included in the meta-analysis.



**Figure 2.** Short-term mortality risk ratio. Forest plot of short-term mortality in acute coronary syndromes with or without concomitant COVID-19 infection, demonstrating an overall risk ratio of 5.34 (95% confidence intervals 4.84–5.90) in the COVID group. The funnel plot indicates low heterogeneity among the included studies.

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1 May 2022

Available online 13 June 2022