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EDITORIAL COMMENT: Expert Article Analysis for:
Coding the COVID patient: Is it futile?

Outcomes of in-hospital cardiac arrest in COVID-19 patients: A proportional prevalence meta-analysis

Tanveer Mir MD[1] | Yasar Sattar MD[2] | Javeed Ahmad[3] | Waqas Ullah MD[4] | Layla Shanah MD[1] | M Chadi Alraies MD[5] | Waqas T. Qureshi MD, MS[6]

[1]Department of Internal Medicine, Wayne State University, Detroit Medical Center, Detroit, Michigan
[2]Internal Medicine, Icahn School of Medicine at Mount Sinai Elmhurst Hospital, Queens, New York, New York
[3]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
[4]Abington Jefferson Health, Abington, Pennsylvania
[5]Cardiovascular Institute, Detroit Medical Center, Detroit, Michigan
[6]University of Massachusetts School of Medicine, Worcester, Massachusetts

Correspondence
Waqas T. Qureshi, University of Massachusetts School of Medicine, Worcester, MA 01655.
Email: waqas.qureshi@umassmed.edu

Abstract

Background: Limited epidemiological data are available on the outcomes of in-hospital cardiac arrest (CA) in COVID-19 patients.

Methods: We performed literature search of PubMed, EMBASE, Cochrane, and Ovid to identify research articles that studied outcomes of in-hospital cardiac arrest in COVID-19 patients. The primary outcome was survival at discharge. Secondary outcomes included return of spontaneous circulation (ROSC) and types of cardiac arrest. Pooled percentages with a 95% confidence interval (CI) were calculated for the prevalence of outcomes.

Results: A total of 7,891 COVID patients were included in the study. There were 621 (pooled prevalence 8%, 95% CI 4–13%) cardiac arrest patients. There were 52 (pooled prevalence 3.0%; 95% CI 0.0–10.0%) patients that survived at the time of discharge. ROSC was achieved in 202 (pooled prevalence 39%;95% CI 21.0–59.0%) patients. Mean time to ROSC was 7.74 (95% CI 7.51–7.98) min. The commonest rhythm at the time of cardiac arrest was pulseless electrical activity (pooled prevalence 46%; 95% 13–80%), followed by asystole (pooled prevalence 40%; 95% CI 6–80%). Unstable ventricular arrhythmia occurred in a minority of patients (pooled prevalence 8%; 95% CI 4–13%).

Conclusion: This pooled analysis of studies showed that the survival post in-hospital cardiac arrest in COVID patients is dismal despite adequate ROSC obtained at the time of resuscitation. Nonshockable rhythm cardiac arrest is commoner suggesting a non-cardiac cause while cardiac related etiology is uncommon. Future studies are needed to improve the survival in these patients.

KEYWORDS
COVID-19, in-hospital cardiac arrest, mortality, pulseless electrical activity

1 | INTRODUCTION

Coronavirus disease 2019 (COVID), a pandemic that initiated from Wuhan, China is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). It was acknowledged as an international public health emergency by the World Health Organization on 30 January 2020.[1,2] The clinical manifestations vary from asymptomatic to severe multiorgan dysfunction and death.[2] Cardiopulmonary resuscitation (CPR) is recommended for cardiac arrest in COVID patients as is in non-COVID patients with some differences in recommendations considering the high infectious rate of COVID-19 infection.[3] American Heart Association CPR guidelines recommended proper donning with protecting gear of health care workers before starting CPR of COVID patients.[4] The outcomes of in-hospital-cardiac arrest postresuscitation in non-COVID patients has improved over last two decades and mostly depends on the quality of CPR performed.[5] Rate of compressions, depth of compression, and rate of ventilations determine the overall survival postcardiac arrest.[6] The data on post-cardiac arrest outcomes in COVID-patients is very limited. Therefore, we aimed to meta-analyze studies that examined in-hospital cardiac arrest in COVID patients.

2 | METHODS

2.1 | Search strategy

Our meta-analysis was performed using the standard protocol devised by the "Meta-analysis of Observational Studies in Epidemiology (MOOSE)". Electronic databases including MEDLINE (PubMed and Ovid), Google scholar, and clinicaltrial.org were searched using a combination of medical subject headings and key terms like "in-hospital" "cardiac arrest" "coronavirus" and "COVID" (Data S1). A cross-reference check of previously published articles on this topic was also performed. The full text of potentially relevant articles was read by the two authors (Tanveer Mir and Javeed Ahmad). Disagreements were resolved by consensus. All extracted data from the included studies were collected into a spreadsheet and verified by a third author (Yasar Sattar). The search was restricted to English literature published from inception of database till November 2020. Only studies with adult patients ≥18 years of age and reported outcome of in-hospital cardiac arrest for COVID patients, who had cardiopulmonary resuscitation, were included in this meta-analysis. Studies with insufficient data, case reports, duplicate data and review articles were excluded. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed to obtain studies for quantitative analysis (Figure 1; Research checklist).

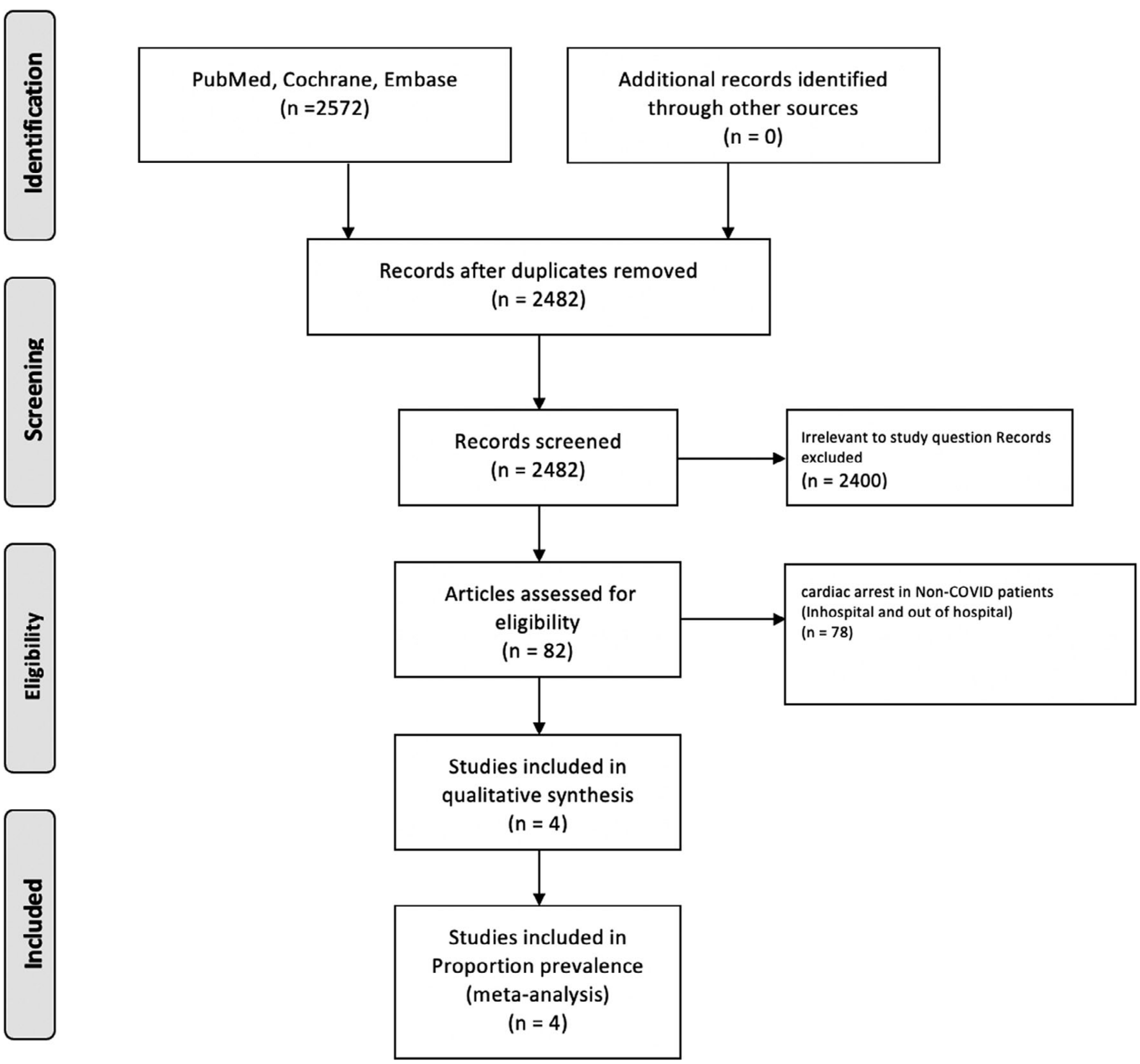

FIGURE 1 PRISMA flow chart for selection of studies[7]

2.2 | Data extraction

Data was collected for (a) baseline characteristics: age, sex, hypertension, diabetes mellitus, pulmonary disease, and chronic kidney disease; (b) baseline rhythm at the time of cardiac arrest, pulseless electrical activity (PEA), ventricular tachycardia (VT)/ventricular fibrillation (VF), and asystole; and (c) outcome measures including ROSC and survival at discharge were recorded. Corresponding authors of studies included in this meta-analysis were contacted for any missing data. Cardiac arrest was defined as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation and ROSC is defined for all rhythms as the restoration of a spontaneous perfusing rhythm that results in more than an occasional gasp, fleeting palpated pulse, or arterial waveform.[8] All outcomes were studied for the hospital stay and hence follow-up was not required. There was no direct patient or public involvement in our study.

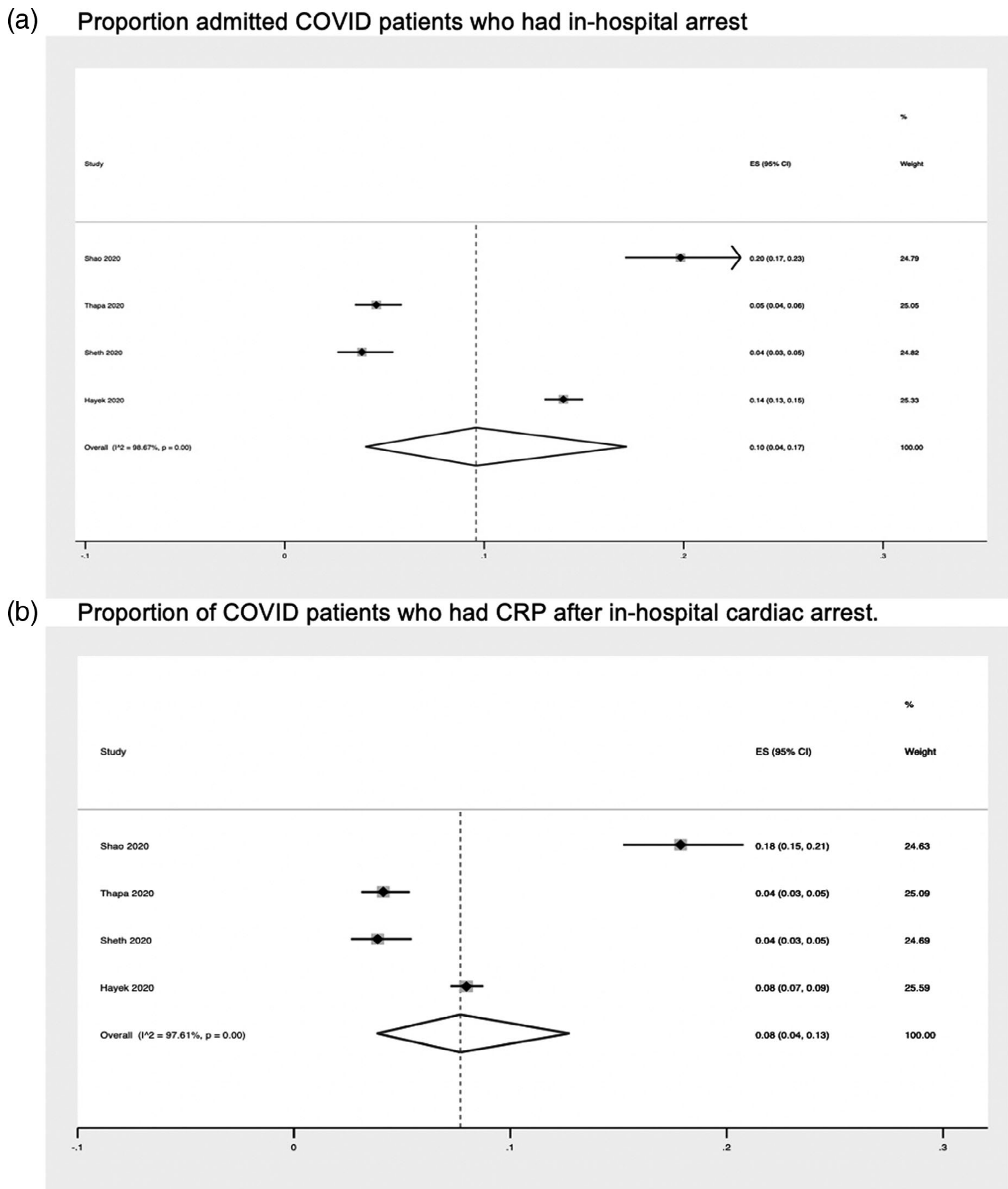

FIGURE 2 (a) Proportion admitted COVID patients who had in-hospital arrest. (b) Proportion of COVID patients who had CRP after in-hospital cardiac arrest

TABLE 1 Baseline characteristics of the studies and baseline cardiac rhythm at the time of arrest

Study	Country	n	Male n (%)	Hypertension n (%)	Diabetes n (%)	Pulmonary disease n (%)	CKD n (%)	VT/VF n (%)	PEA n (%)	Asystole n (%)
Shao et al	China	136	90 (66.2)	41 (30.2)	27 (19.9)	6 (4.4)	3 (2.2)	8 (5.9)	6 (4.4)	122 (89)
Thapa et al	USA	54	33 (61.1)	42 (77.1)	50 (55.6)	–	–	2 (3.7)	44 (81.5)	8 (14.8)
Sheth et al	USA	31	22 (71)	–	13 (42)	13 (42)	6 (19)	4 (13)	18 (58)	9 (29)
Hayek et al	USA	400	266 (66.5)	253 (63.2)	201 (50.2)	31 (7.8)	84 (21)	48 (12)	199 (49.7)	95 (23.8)

Abbreviations: CKD, chronic kidney disease; PEA, pulseless electrical activity; USA, United States of America; VT, ventricular tachycardia; VF, ventricular fibrillation.

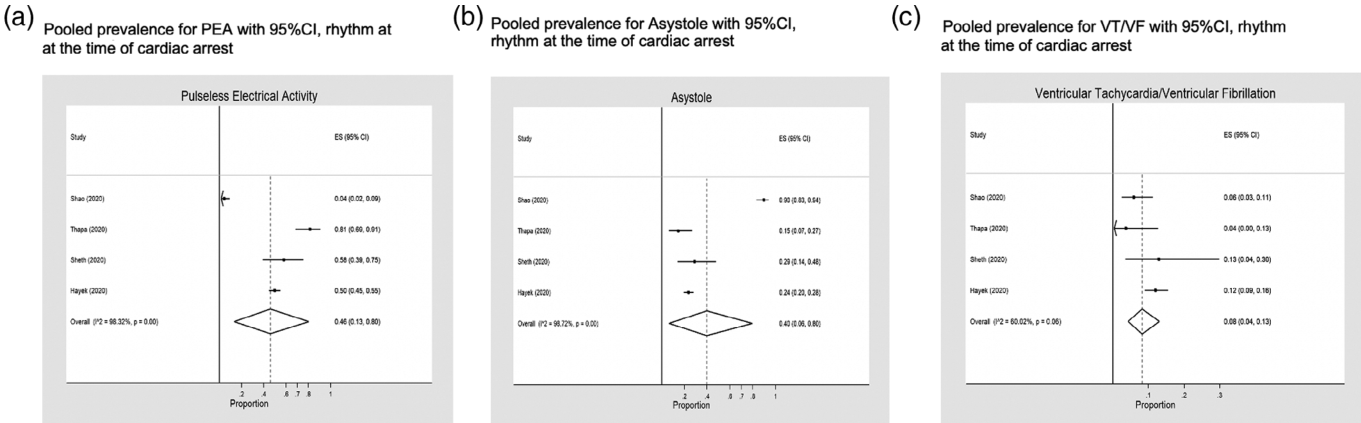

FIGURE 3 (a) Pooled prevalence for PEA with 95%CI, rhythm at the time of cardiac arrest. (b) Pooled prevalence for Asystole with 95%CI, rhythm at the time of cardiac arrest. (c) Pooled prevalence for VT/VF with 95%CI, rhythm at the time of cardiac arrest

2.3 | Statistical analysis

Baseline characteristics were obtained from review of the included studies. Continuous variables from the studies were pooled and mean estimates along with standard errors were calculated. Pooled estimates of the prevalence rates for the types of in-hospital cardiac arrest for COVID patients were calculated. All analyses were carried out using Stata (version 16.0). Meta-analyses were performed adopting a Stata modules, Metan, and Metaprop, designed to perform meta-analyses of proportions.[9] Random effect model was used for calculation of the prevalence. The random effects model assumes that the studies included in the meta-analysis are a random sample of hypothetical study populations. The estimated pooled prevalence was reported as pooled percentage with 95% confidence interval (CI). An alpha criterion of *P* value <.05 was considered statistically significant. Higgins *I*-squared (I^2) statistical model was used to evaluate variations in outcomes of included studies. I^2 values of 50% or less corresponded to low to moderate, and 75% or higher indicated large amounts of heterogeneity. The methodological quality was performed by screening all included articles for different types of bias (selection, ascertainment, causality, and reporting) and evaluated as per the modified tool for quality assessment for case series.[10]

3 | RESULTS

3.1 | Search results and study characteristics

Initial search identified 2,572 articles. After exclusion of duplicates (*n* = 2,482) and irrelevant (*n* = 2,400) articles, 82 studies were found relevant to the review. Out of these, 78 studies were excluded as studies were in non-COVID patients evaluating in-hospital and out of hospital cardiac arrest. Four studies qualified for quantitative analysis. The detailed PRISMA flow diagram is shown in Figure 1.

The included studies included a total of 7,891 COVID patients. In-hospital cardiac arrest occurred in 943 (pooled prevalence 10%, 95% CI 4–17%; Figure 2) and 621 (pooled prevalence 8%, 95% CI 4–13%) underwent CPR that were included in this study. The mean age was 62 ± 11 years and mostly were males (*n* = 411) 66.2%. Mean prevalence of comorbidities are given in comorbidities are given in Table 1.

3.2 | Prevalence of outcomes

The commonest initial rhythm at the time of cardiac arrest was PEA followed by asystole and ventricular arrhythmia (Figure 3). Out of

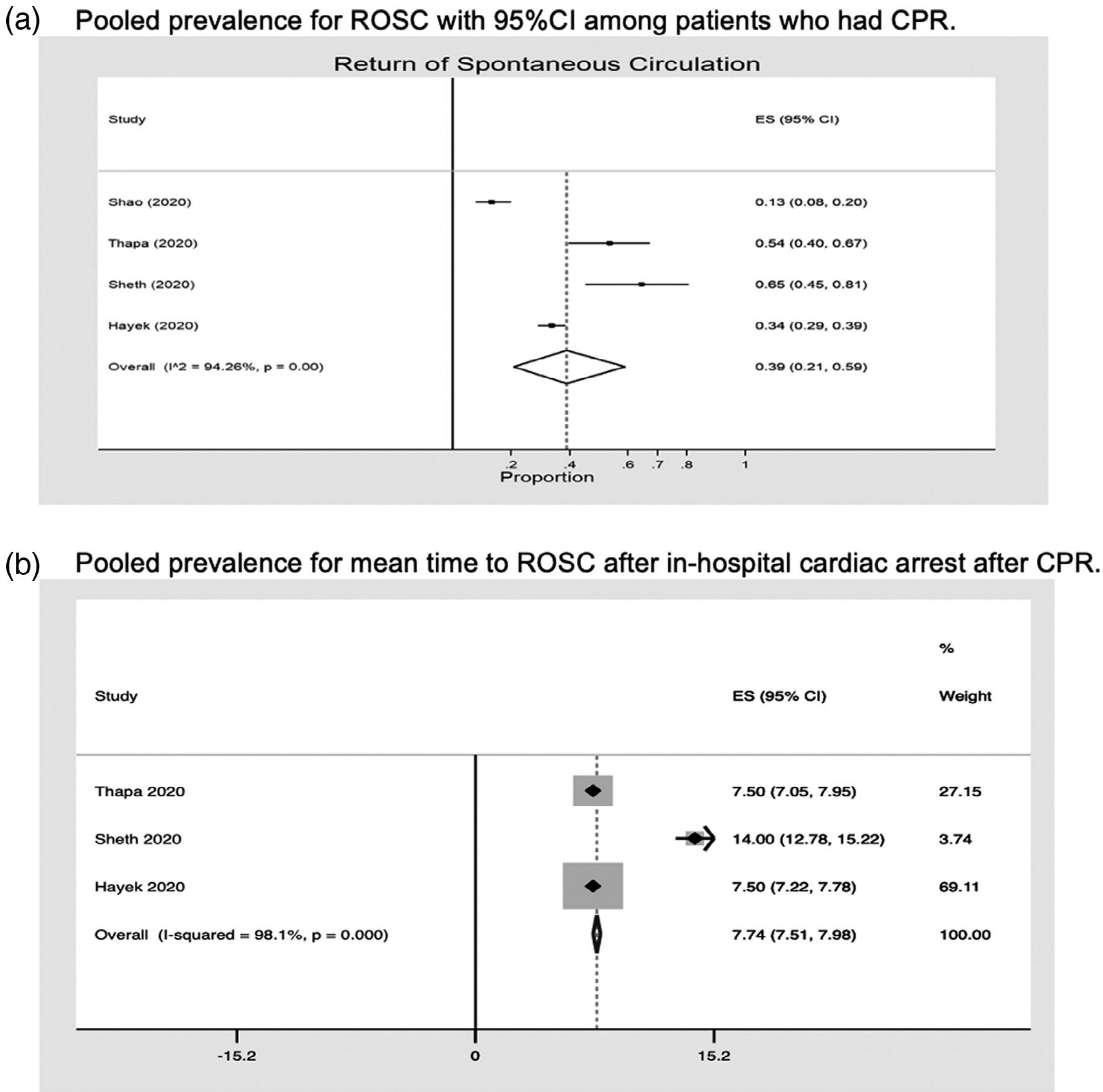

FIGURE 4 (a) Pooled prevalence for ROSC with 95%CI among patients who had CPR. (b) Pooled prevalence for mean time to ROSC after in-hospital cardiac arrest after CPR

621 cardiac arrest patients, ROSC was achieved in 202 patients (pooled prevalence 39%; 95% CI 21–59%; Figure 4). Mean time to ROSC was 7.74 (95% CI 7.51–7.98) min (Figure 4). Despite significant prevalence of ROSC, there were only 52 patients (pooled prevalence 3%; 95% CI 0–10%). There were 569 deaths (pooled mortality rate 7%, 95% CI 4–12%) (Figure 5).

3.3 | Quality of the included studies

All the included studies were observational retrospective studies.[11-14] The studies were assessed for selection, representation, exposure and outcome adequacy, causality and reporting. Mean quality score was 6 (Table S1).

4 | DISCUSSION

In this meta-analysis of COVID patients, we observed that every 10th patient suffered from in-hospital cardiac arrest and every 14th patient did not leave the hospital alive. Even though, ROSC was achieved among 2/5th of these patients, only a very small proportion left the hospital alive suggesting dismal survival in these patients that suffer from in-hospital cardiac arrest. We also observed that most of these cardiac arrests had nonshockable initial rhythm. There was a significant comorbidity burden in these patients as well.

Our study revealed pooled prevalence of in-hospital mortality for COVID patients was double (7%) than the reported mortality rate for COVID infections in USA.[15,16] The survival at discharge was dismal (3% of cardiac arrest patients that underwent CPR) for these patients

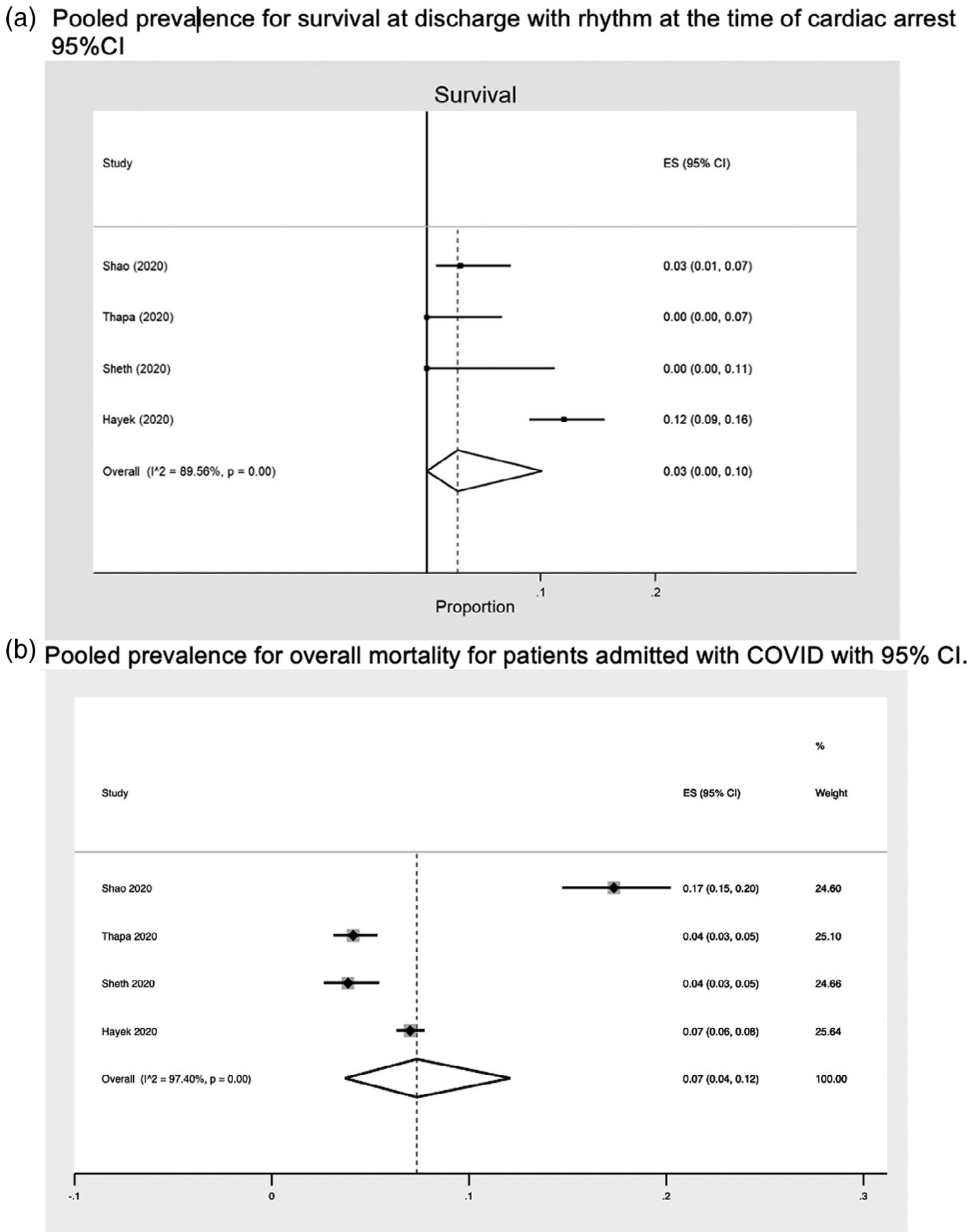

FIGURE 5 (a) Pooled prevalence for survival at discharge with rhythm at the time of cardiac arrest. 95%CI. (b) Pooled prevalence for overall mortality for patients admitted with COVID with 95% CI

that suffered from in-hospital cardiac arrest. Prior studies in non-COVID patients report rates of survival in the range of 13.7 in 2000 and increased to 22.3% in 2009 at the time of discharge.[17] A study by Ehlenbach et al reported a survival outcome of 18.3% at discharge in non-COVID patients who had cardiac arrest within hospital.[18] The improvement in survival outcomes over last two decades were secondary to improvement in quality of CPR and defibrillation within seconds to minutes.[19] Prior studies also report much higher degree of ROSC for in-hospital cardiac arrest within the range of 48–84%.[17,20-23] We observed a much lower rate of ROSC in these patients. We suspect that one of the contributing factors for the high mortality rates and lower ROSC rates could be secondary to delay in CPR due to donning personal protective equipment or inexperienced staff performing CPR during the crisis period as a result of unavailability of experienced staff.[24] Delayed and prolonged CPR has independent and inverse relation with outcome of cardiac arrest.[25,26] Interestingly Hayek et al reported low median time for ROSC and better outcomes for cardiac arrest than other studies. Despite this the mean time to achieve ROSC was within 10 min.

Poor insight into the disease could be another reason for poor outcome in COVID patients.[24] Two of the studies included in our meta-analysis had no survival at disease were with patient population from March to May when COVID pandemic was in early phases.[11,13] Hayek et al[14] had the quickest time to ROSC with highest survival at discharge that included patients from March–June when the availability for protective gear became more widespread than the initial phase of pandemic.

Interestingly, age and comorbidity profile are an important predictor of outcome of cardiac arrest. Severe COVID is associated with high comorbidity profile and advanced age and hence poor outcome.[27] Our pooled analysis also found a higher prevalence of cardiac arrest in advanced age.[11-14] Majority of these patients had multiple comorbidities. This could be another etiology of poor outcome that we observed in this study.

In addition, our study revealed a higher prevalence of PEA and asystole at the time of cardiac arrest in COVID patients. PEA had a prevalence of 46% and asystole 40% as the baseline rhythm of cardiac arrest. Shockable rhythm was present in minority of the patients. Nonshockable rhythm (PEA and asystole) has shown to be associated with lower survival rates.

There are several implications of this study. First, this study provides us insight into the higher mortality rate of COVID patients with in-hospital cardiac arrest. This could be due to logistic reasons and suggests further research into this particular issue. Second, the study also provides significantly dismal survival rate among patients that developed in-hospital cardiac arrest that could help in leading goals of care discussion with the families in these patients. Third, we observed that studies with quicker ROSC had better survival rate suggesting the need for protocoling quicker resuscitation measures in these patients. Certain devices are now available to provide effective CPR and could provide no-contact CPR to these patients without leading to additional aerosol risk to the resuscitation team.[28]

Our study is constrained by the limitations of the included studies. Systematic reviews are potentially susceptible to publication bias. We attempted to limit the potential for publication bias by conducting an extensive search for all relevant publications reporting prevalence or providing data from which prevalence can be calculated. The data about the quality of CPR could not be accessed. Shoa et al did not reveal time to ROSC.

5 | CONCLUSION

The survival at discharge for in-hospital cardiac arrest remains dismal despite acceptable rate of ROSC obtained after resuscitation efforts. The commonest rhythm at the time of arrest was nonshockable rhythm. Further research is needed to improve survival in these patients that were adequately resuscitated at the time of cardiac arrest.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Waqas Ullah https://orcid.org/0000-0002-4850-0309
M Chadi Alraies https://orcid.org/0000-0002-7874-4566
Waqas T. Qureshi https://orcid.org/0000-0002-5189-4417

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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