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Unraveling the Consequences of the COVID-19 Pandemic on Out-of-hospital Cardiac Arrest: A Systematic Review and Meta-analysis

Miroslaw Dabkowski[1], Damian Swieczkowski[2], Michal Pruc[3], Başar Cander[4], Mehmet Gül[5], Nicola Bragazzi[6], Lukasz Szarpak[7]

[1]Polish Society of Disaster Medicine, Research Unit, Warsaw, Poland
[2]Medical University of Gdansk Faculty of Pharmacy, Department of Toxicology, Gdansk, Poland
[3]International Academy of Ecology and Medicine, Department of Public Health, Kyiv, Ukraine
[4]Bezmialem Vakıf University Faculty of Medicine, Department of Emergency Medicine, İstanbul, Turkey
[5]Necmettin Erbakan University Faculty of Medicine, Department of Emergency Medicine, Konya, Turkey
[6]York University, Laboratory for Industrial and Applied Mathematics (LIAM), Department of Mathematics and Statistics, Toronto, Canada
[7]Baylor College of Medicine, Henry JN Taub Department of Emergency Medicine, Houston, USA

Abstract

Aim: The aim of this systematic review and meta-analysis was to assess the influence of the Coronavirus disease-2019 (COVID-19) pandemic on the incidence, characteristics, and clinical consequences of out-of-hospital cardiac arrest (OHCA).

Materials and Methods: We searched PubMed, Embase, Scopus, Web of Science, and Cochrane Library databases up to May 30, 2023 for studies containing comparative data of OHCA patients in COVID-19 and pre-pandemic periods.

Results: A total of 35 articles concerning to 34 studies screening based on the inclusion criteria. COVID-19 was associated with higher incidence of OHCA at home compared with the pre-pandemic period ($p<0.001$), longer emergency medical services arrival time ($p<0.001$), longer on-scene time ($p<0.001$), as well as reduction of shockable rhythms ($p=0.02$). COVID-19 compared with the pre-pandemic period was associated with lower survival to hospital admission (11.2% vs. 19.3%; $p<0.001$). Survival to hospital discharge (SHD) was 4.8% vs. 12.9%, respectively ($p<0.001$), while SHD with a good neurological outcome also varied and amounted to 3.6% vs. 5.8%, respectively ($p<0.001$).

Conclusion: COVID-19, compared with the pre-pandemic period, was characterized by a reduced rate of defibrillation rhythms during OHCA, as well as a worse prognosis in terms of both survival to hospital admission, SHD, and SHD good neurological outcome.

Keywords: Out-of-hospital cardiac arrest, OHCA, outcome, survival, SARS-CoV-2, COVID-19

Introduction

Out-of-hospital cardiac arrest (OHCA) is defined as a sudden and unexpected stop of heart function occurring outside a professional setting, e.g., a hospital or other healthcare facility, with visible signs of an abrupt absence of circulation. In most cases, OHCA is caused by cardiac causes, such as progressive heart failure, arrhythmias, and sudden coronary episodes. In the case of noncardiac causes, multiple organ injuries and drug overdoses are common causes of OHCA (1). Unfortunately, despite the progress of knowledge and techniques, the prognosis after OHCA remains poor, with only a 22% survival rate to hospital admission and an 8.8% survival rate to hospital discharge. The long-term prognosis remains unsatisfactory, with a 1-year survival rate of 7.7%; based on pre-Coronavirus disease-2019 (COVID-19) data (2). High mortality is associated with poor neurological conditions after OHCA. A very low left ventricular ejection fraction is also a predictor of high mortality (3,4). Disability, which affects a

Corresponding Author: Lukasz Szarpak MD, Baylor College of Medicine, Henry JN Taub Department of Emergency Medicine, Houston, USA
Phone: +48500186225 **E-mail:** lukasz.szarpak@gmail.com **ORCID ID:** orcid.org/0000-0002-0973-5455

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significant proportion of OHCA survivors, is a significant burden on the health and social care systems (5).

The COVID-19 pandemic caused by the Severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) has had a profound impact on various aspects of global public health (6-8). Based on the so far published data, we can assume that the situation worsened during the COVID-19 pandemic. Several factors have contributed to a significant impact on OHCA outcomes during the COVID-19 pandemic (9). Some issues affecting OHCA outcomes were identified before the pandemic. However, it was the pandemic that exaggerated their impact on OHCA outcomes. Staff shortages could result in delayed response times for OHCA cases, e.g., increasing the time needed for emergency services to arrive at the scene. Some analysts have suggested that indicators such as survival to hospital admission and survival discharge decreased compared with pre-pandemic data (10,11). The limited availability of critical care resources, such as intensive care unit beds and specialized cardiac care, has also been observed during the pandemic (12). Not to mention the impact of limited resource availability during the pandemic on post-resuscitation care, such as neurological rehabilitation, on OHCA outcomes, particularly from a long-term perspective (13).

Because the prognosis, both short- and long-term, after OHCA correlates with the rapidity of starting cardiopulmonary resuscitation (CPR) by bystanders, the fear of SARS-CoV-2 virus transmission may have prevented people from providing first aid (14-17). In addition, limited access to the health care system, sometimes also due to fear of potential infection, led to exacerbation of underlying diseases, contributing to both an increase in new OHCA incidents and equally contributing to a more negative prognosis (18-20). The impact of COVID-19 on pre-existing underlying diseases, particularly cardiovascular disease, should be mentioned. In general, people with chronic disease, particularly cardiovascular disease, have a worse prognosis when OHCA as well as in-hospital cardiac arrest develop (21-23). In addition, people with increased cardiovascular risk (pre-existing) have contracted COVID-19, they are at an increased risk of OHCA (24). In addition, both the access to and frequency of use of the automated external defibrillator (AED) decreased during the pandemic, which could also potentially contribute to the worsening of OHCA outcomes (25).

Considering the above, the goal of this study was to conduct a systematic review and meta-analysis to assess the influence of the COVID-19 pandemic on the incidence, characteristics, and clinical consequences of OHCA. The major hypothesis is that the pandemic era is linked with an increased incidence of OHCA and a higher case fatality rate compared with the pre-pandemic period. Furthermore, it is hypothesized that intermediate clinical outcomes such as ROSC, survival to hospital admission, and survival to hospital release have fallen throughout the epidemic. Furthermore, this study intends to investigate changes in the etiologies of OHCA throughout the pandemic as well as a possible decrease in the rate of shockable rhythm as the initial presenting rhythm.

Materials and Methods

To create this publication, we followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) Statement Guidelines (26), and the PRISMA checklist is provided as supplemental digital content. Before beginning this investigation, a review procedure was registered in PROSPERO (reference: CRD42022382144).

Search Strategy

Two investigators (M.D. and M.P.) independently systematically searched the PubMed, EMBASE, Scopus, Web of Science, and Cochrane Library databases for relevant articles from database inception to May 30, 2023. The consensus of all authors resolved any disagreement or conflict. For each database, a specific and effective search method was employed. We used the following searching terms: "OHCA" or "out-of-hospital cardiac arrest" OR "out of hospital cardiac arrest" OR "sudden cardiac death" OR "heart arrest" OR "cardiac arrest" OR "sudden cardiac death" OR "cardiopulmonary arrest" AND "SARS-CoV" OR "severe acute respiratory syndrome coronavirus 2" OR "COVID-19" OR "novel coronavirus" OR "nCOV".

Google and Google Scholar were also utilized as search engines. A manual search of the article references was also carried out. To combine search results, Endnote (X7 for Windows, Clarivate Analytics, Philadelphia, PA, USA) was utilized, and duplicates were removed.

Eligibility Criteria

Two investigators (M.D. and M.P.) independently reviewed all retrieved publications in comparison to predetermined selection criteria. The consensus of all writers resolved any controversy or inconsistency. From December 2019 to May 2023, we included publications published as systematic meta-analysis research in peer-reviewed journals in full text in English, Polish, or Spanish. Inclusion criteria also included: (1) studies comparing OHCA outcomes before and during the COVID-19 era or during the COVID-19 period; (2) studies evaluating cardiac arrest clinical outcomes; and (3) studies having accessible and necessary data. Articles must also have a defined method for conducting literature searches. (1) reviews, conference abstracts, pediatric patients, animal experiments, case reports or case series, or comments were excluded; (2) the publication was not published in English, Polish, or Spanish; and (3) basic data could not be collected.

Data Extraction

Two authors (M.D. and L.S.) independently extracted data into standardized spreadsheets using Excel (Microsoft Corp., Redmond, WA, USA) format. The following information was extracted: A) study characteristics (i.e., first author name, year of publication, study origin, study design); B) participant characteristics (i.e., number of participants, age, male gender); C) OHCA characteristics (i.e., location of cardiac arrest, OHCA etiology, witnessed cardiac arrest, bystander CPR, AED application); D) ACLS characteristics (i.e., medicaments application; TTM; defibrillation; ACCD application; shockable rhythm, emergency medical services (EMS) arrival time, on scene time); D) outcomes [i.e., survival to hospital admission; survival to hospital discharge (SHD) or 30-day survival rate, SHD with good neurological outcome]. Disagreements were resolved through discussion and consensus with other authors.

Publication Bias Assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included trials using an eight-item score split into three areas (27). These areas evaluate the selection, comparability, and ascertainment of the desired outcome. The quality assessment of articles ranged from low scores (0-4) to moderate scores (5-6) to high scores (7-9), representing three different levels of study quality. The two reviewers (M.D. and B.C.) utilized NOS to independently assess the quality of the studies and the risk of bias. Each reviewer utilized the same set of judgment procedures to rate the research. A third author evaluated and resolved any differences with the NOS.

Outcomes

The primary endpoint of the study was SHD/30-day survival rate. Secondary outcomes were: survival to hospital admission, defined as admission with a pulse; SHD with a good neurological outcome [defined according to Cerebral Performance Categories (CPC) score 1 or 2].

Statistical Analysis

Review Manager (version 5.4, Nordic Cochrane Centre, Cochrane Collaboration, UK) and STATA 16.0 (StataCorp LLC, Texas, US) were used for statistical analyzes statistical significance was determined as a two-tailed p-value of less than 0.05. The results are displayed as forest plots with 95% confidence intervals (CIs) using odds ratios (ORs) for dichotomous data and mean difference for continuous data. When data were presented as medians with an interquartile range, Hozo's algorithm was used to calculate estimated means and standard deviations (28). The I^2 test was used to analyze study heterogeneity, which was classified as low, moderate, or high when I^2 was 50%, 50-75%, or 76%, respectively (29). Regardless of heterogeneity, random effect models were applied. To verify the robustness of the findings, sensitivity analysis employing leave-one-out was undertaken. Egger's test and funnel plots were used to investigate publication bias (30). When at least ten papers were included in the meta-analysis, publication bias was assessed using funnel plots (31).

Results

The search process yielded a total of 1271 articles. Due to duplication, 623 papers were discarded and 648 articles were further excluded following a preliminary evaluation of titles and abstracts, resulting in 67 research articles. Twenty five of these papers shared study data with other articles or relevant data could not be obtained, and 10 articles presented no original data. A final total of 35 articles concerning 34 studies screening based on the inclusion criteria (10,18,32-64). Figure 1 depicts the work flow of the study selection procedure.

Characteristics of Included Studies

The 34 studies involved 144,971 OHCA adults. They were published between 2020 and 2023 and were performed in USA, Korea, Thailand, Taiwan, France, Italy, Switzerland, Australia, UK, China, Spain, Germany, Sweden, Canada and Singapore. A graphical summary of studies from each country is shown in Figure 2. Their overall quality was good, where eleven studies

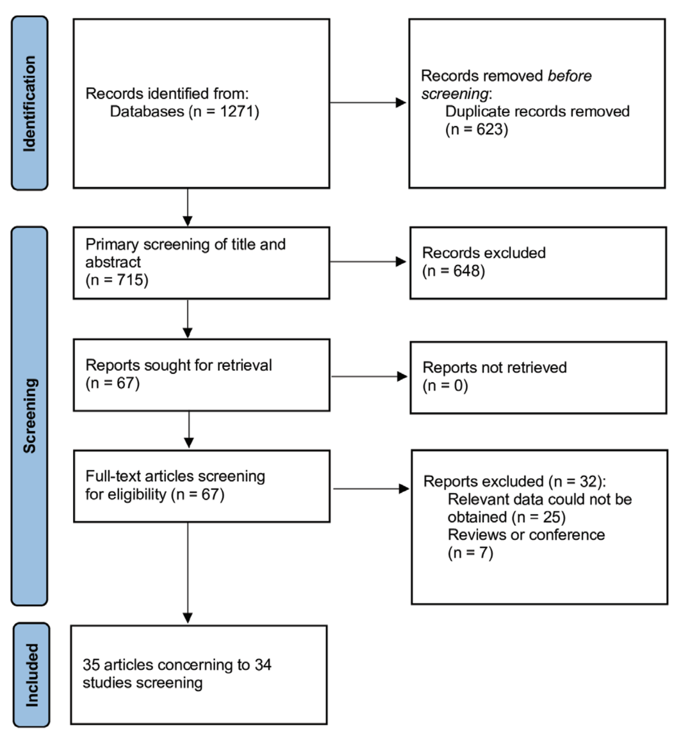

Figure 1. Flow diagram of the search strategy and study selection

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scored 9/9 on the NOS, eighteen studies scored 8/9, and five studies scored 7/9 (Table 1).

The mean age of OHCA patients in the COVID-19 group was 69.4±15.1 years, compared to 68.6±16.3 years for patients from the pre-COVID-19 period (p=1.0). Men made up 57.9% of the group of patients with OHCA in the COVID-19 period, compared to 60.6% in the pre-COVID-19 period (p=0.52).

Characteristics of the Resuscitation Process

COVID-19 was associated with a higher incidence of OHCA at home compared with the pre-pandemic period (88.1% vs. 78.8%; p<0.001).

COVID-19 compared to the pre-pandemic period was associated with increased EMS arrival time (10.3±5.5 vs. 10.1±3.6 min, p<0.001), on-scene time (18.9±8.6 vs. 18.5±7.4 min, p<0.001), and first defibrillation time (14.7±4.9 vs. 12.5±4.3 min, p<0.001). In addition, a statistically significant reduction of 6.2% in the incidence of shockable rhythm was observed during COVID-19 (p=0.02). The summary of the risk of bias in each of the included studies is listed in Table 2.

Outcomes

Twenty-nine trials reported survival to hospital admission. Pooled analysis of SHA among the COVID-19 period and the pre-pandemic period varied and amounted to 11.2% vs. 19.3% (OR=0.75; 95% CI: 0.65 to 0.85; p<0.001; Figure 3).

SHD was reported in twenty-six studies and was 4.8% in the pandemic period, compared to 12.9% for OHCA patients in the pre-COVID-19 period (OR=0.54; 95% CI: 0.45 to 0.65; Figure 4).

Thirteen studies reported SHD with a good neurological outcome. Pooled analysis showed that SHD with CPC 1-2 was 3.6% in the COVID-19 period, compared to 5.8% for the pre-COVID-19 period (OR=0.61; 95% CI: 0.51 to 0.73; p<0.001; Figure 5).

Discussion

This publication presents a systematic review and meta-analysis examining the impact of the COVID-19 pandemic on outcomes of OHCA patients and includes 34 studies involving a substantial sample size of 144,971 OHCA adults from various countries.

One of the key findings of this study is the higher incidence of OHCA at home during the COVID-19 period compared with the pre-pandemic period. This shift in OHCA location may be attributed to factors such as lockdowns, reduced mobility, avoidance of healthcare facilities, and delayed seeking of medical care due to fear of contracting COVID-19 (65). The home environment presents unique challenges for resuscitation efforts, including potential delays in bystander CPR and limited access to early defibrillation, which can impact survival rates (46).

Another important finding is the increase in EMS arrival time, on-scene time, and the first defibrillation time during the COVID-19 period. The pandemic has placed an unprecedented burden on healthcare systems worldwide (1,10,12). EMS providers have been stretched thin, facing increased call volumes and demands for COVID-19-related care (68). This surge in workload and resource allocation may result in delayed EMS arrival times, as ambulances may be occupied with other emergency calls or COVID-19-related tasks (69).

In response to the highly transmissible nature of the SARS-CoV-2 virus, EMS providers have had to implement additional infection prevention measures to protect themselves and their patients. These measures, such as donning personal protective

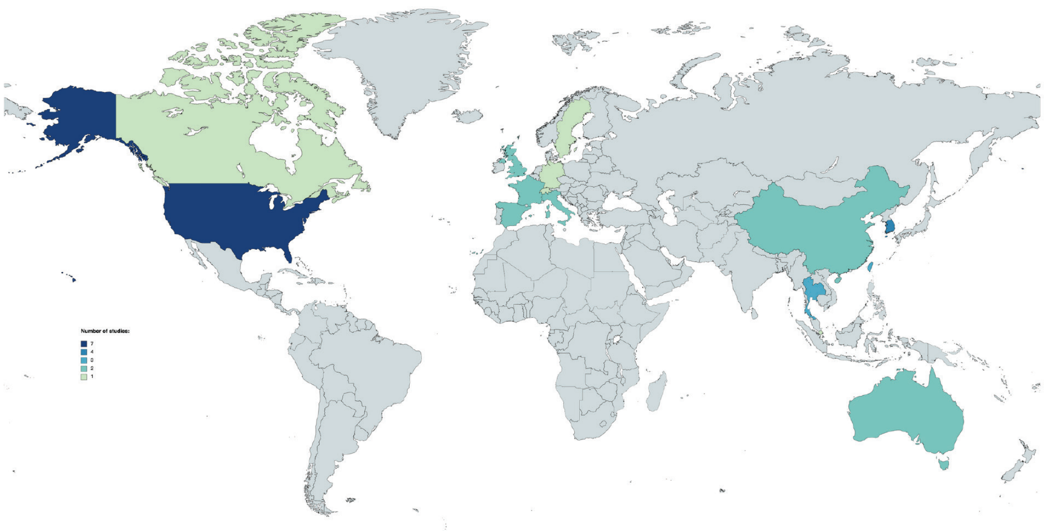

Figure 2. Country origin of studies included in the meta-analysis

Table 1. Baseline characteristics of included trials

Study	Country	Study design	Pre-COVID-19 period			COVID-19 period			NOS score
			No.	Age	Male sex	No.	Age	Male sex	
Ahn et al., 2021 (32)	Korea	Prospective study	145	72.9±3.4	91 (62.8%)	152	74.95±2.6	102 (67.1%)	8
Baert et al., 2020 (33)	France	The comparative multicentre study	1620	69±17	1071 (66.1%)	1005	68±17	676 (67.3%)	8
Baldi et al., 2020 (34)	Italy	Multicentre longitudinal prospective registry	321	77.8±3.2	188 (58.6%)	490	76.8±2.8	321 (65.5%)	9
Baldi et al., 2021 (35)	Switzerland	Population-based observational study	933	70.5±4	636 (68.2%)	911	69±4	623 (68.4%)	8
Ball et al., 2020 (36)	Australia	The retrospective cohort study	1218	66±4.3	845 (69.4%)	380	68±4.3	250 (65.8%)	8
Biskupski et al., 2022 (37)	USA	The single-center cohort study	28	NS	17 (60.7%)	86	NS	52 (60.5%)	7
Breglia et al., 2022 (38)	Italy	Retrospective observational study	64	71.3±17.3	46 (71.9%)	50	71.1±14.3	35 (70.0%)	7
Burns et al., 2022 (39)	USA	Retrospective chart review	499	67.6±20.6	293 (58.7%)	617	67.2±19.9	376 (60.9%)	8
Chavez et al., 2022 (10)	USA	Retrospective chart review of the cardiac arrest registry	3619	62.8±3.8	2307 (63.8%)	4418	63.8±3.8	2781 (63.0%)	8
Cho et al., 2020 (40)	Korea	Retrospective observational study	158	72.5±3	103 (65.2%)	171	73.2±3.4	108 (63.2%)	8
Chugh et al., 2022 (41)	USA	Prospective, population-based study	1315	71.3±15.8	857 (65.2%)	907	69.5±17.0	586 (64.6%)	8
Chung et al., 2022 (42)	Korea	The retrospective cohort study	129	71.2±14.6	79 (61.2%)	101	68.2±17.8	65 (64.4%)	8
Fothergill et al., 2021 (43)	UK	Retrospective observational study	1724	68±20	1069 (62.0%)	3122	71±19	1839 (59.0%)	9
Huabbangyang et al., 2023 (44)	Thailand	Retrospective observational study	513	64.18±19.94	320 (62.4%)	482	65.18±18.16	304 (63.1%)	8
Lai et al., 2020 (45)	USA	Population-based, cross-sectional study	1336	68±19	752 (57.1%)	3989	72±18	2183 (55.8%)	9
Leung et al., 2023 (46)	China	The retrospective cohort study	1502	76.8±4.2	844 (56.2%)	2185	77.7±4.2	1293 (59.2%)	9
Li et al., 2023 (47)	China	Retrospective study	19027	82±3.3	10225 (53.7%)	30962	83.4±3.1	16384 (52.9%)	8
Lim et al., 2021 (48), Cho et al., 2020 (40)	Singapore	The retrospective cohort study	2493	71.1±3.8	1597 (64.1%)	1400	72.5±4	882 (63.0%)	7
Lim et al., 2021 (49)	Korea	Retrospective observational study	891	70.07±15.06	577 (64.8%)	1063	71.05±14.98	647 (60.9%)	9
Liu et al., 2023 (51)	Taiwan	Observational epidemiological analysis	567	75.3±3.5	313 (55.4%)	497	76.5±3.3	292 (59.0%)	9
Marijon et al., 2020 (52)	France	Population-based observational study	30198	68.7±17.9	18668 (60.7%)	519	69.7±17	334 (64.3%)	9
Mathew et al., 2021 (53)	USA	Retrospective study	180	58.5±19.8	93 (51.7%)	291	64.5±18.1	165 (56.7%)	7
Morton et al., 2022 (54)	UK	Retrospective, single-center	147	58.3±3.5	89 (60.5%)	181	51.8±4.5	85 (47.0%)	7
Navalpotro-Pascual et al., 2021 (55)	Spain	Prospective study	306	71.8±3.8	199 (65.0%)	313	71.8±3.2	189 (60.4%)	8
Ortiz et al., 2020 (56)	Spain	Retrospective analysis of prospective registry	1718	65.61±16.9	1208 (70.3%)	1442	64.36±16.5	1027 (71.2%)	8
Phattharapornjaroen et al., 2022 (18)	Thailand	The retrospective cohort study	76	70±17.48	46 (60.5%)	60	65.42±19.43	33 (55.0%)	9
Ristau et al., 2022 (57)	Germany	Epidemiological cross-sectional study	5016	69.7±16.9	3270 (65.2%)	5308	69.7±16.6	3503 (66.0%)	8
Riyapan et al., 2022 (58)	Thailand	Multicentered, retrospective, observational study	341	62.7±18.5	210	350	63.4±19.4	208	9
Sultanian et al., 2021 (59)	Sweden	Observational registry-based study	930	70.8±16.6	604 (64.9%)	1016	69.6±17.8	697 (68.6%)	9
Sung et al., 2022 (60)	Taiwan	The retrospective cohort study	1605	71.3±16.1	969 (60.4%)	1214	70.5±15.7	747 (61.5%)	8
Talikowska et al., 2021 (61)	Australia	The retrospective cohort study	501	60±4.7	345 (68.9%)	145	60.5±4.7	101 (69.7%)	8
Uy-Evanado et al., 2021 (62)	USA	Population-based study	231	69.1±17.4	137 (59.3%)	278	64.9±18.3	174 (62.6%)	8
Yap et al., 2022 (63)	Canada	Observational study	274	46±20	187 (68.2%)	221	43±18	178 (80.5%)	9
Yu et al., 2021 (64)	Taiwan	Retrospective observational study	570	70.93±16.45	353 (61.9%)	622	70.41±16.21	394 (63.3%)	8

NS: Not specified, NOS: Newcastle-Ottawa Scale, COVID-19: Coronavirus disease-2019

Study or Subgroup	Pandemic period Events	Pandemic period Total	Pre-pandemic period Events	Pre-pandemic period Total	Weight	Odds Ratio M-H, Random, 95% CI
Ahn 2021	8	152	25	145	1.7%	0.27 [0.12, 0.61]
Baert 2020	195	999	409	1616	4.3%	0.72 [0.59, 0.87]
Baldi 2020	27	490	44	321	2.8%	0.37 [0.22, 0.61]
Baldi 2021	154	911	166	933	4.1%	0.94 [0.74, 1.20]
Ball 2020	92	380	359	1218	3.9%	0.76 [0.59, 1.00]
Breglia 2022	7	50	9	64	1.2%	0.99 [0.34, 2.89]
Burns 2022	155	617	162	499	4.0%	0.70 [0.54, 0.91]
Chavez 2022	923	4418	981	3619	4.6%	0.71 [0.64, 0.79]
Cho 2020	39	171	49	158	2.9%	0.66 [0.40, 1.07]
Chung 2022	14	101	9	129	1.5%	2.15 [0.89, 5.18]
Fothergill 2021	213	1135	224	683	4.2%	0.47 [0.38, 0.59]
Huabbangyang 2023	134	482	72	513	3.7%	2.36 [1.71, 3.24]
Lai 2020	423	3989	337	1336	4.4%	0.35 [0.30, 0.41]
Leung 2023	453	2185	463	1502	4.4%	0.59 [0.50, 0.68]
Li 2023	600	30962	411	19027	4.5%	0.90 [0.79, 1.02]
Lim 2021 (B)	162	888	200	888	4.1%	0.77 [0.61, 0.97]
Liu 2023	99	497	93	567	3.7%	1.27 [0.93, 1.73]
Marijon 2020	67	521	6925	30247	4.0%	0.50 [0.38, 0.64]
Mathew 2021	32	291	29	180	2.6%	0.64 [0.37, 1.11]
Navalpotro-Pascual 2021	27	313	61	306	2.9%	0.38 [0.23, 0.62]
Phattharapornjaroen 2022	15	60	31	76	1.9%	0.48 [0.23, 1.02]
Ristau 2022	1736	5308	1890	5016	4.6%	0.80 [0.74, 0.87]
Riyapan 2022	45	261	54	254	3.1%	0.77 [0.50, 1.20]
Sultanian 2021	297	1016	310	930	4.3%	0.83 [0.68, 1.00]
Sung 2022	385	1214	545	1605	4.4%	0.90 [0.77, 1.06]
Talikowska 2021	27	145	98	501	2.9%	0.94 [0.59, 1.51]
Uy-Evanado 2021	65	278	74	231	3.3%	0.65 [0.44, 0.96]
Yap 2022	30	221	17	274	2.3%	2.37 [1.27, 4.43]
Yu 2021	126	622	119	570	3.9%	0.96 [0.73, 1.28]
Total (95% CI)		**58677**		**73408**	**100.0%**	**0.75 [0.65, 0.85]**
Total events	6550		14166			

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 251.40$, df = 28 ($P < 0.00001$); $I^2 = 89\%$
Test for overall effect: Z = 4.32 ($P < 0.0001$)

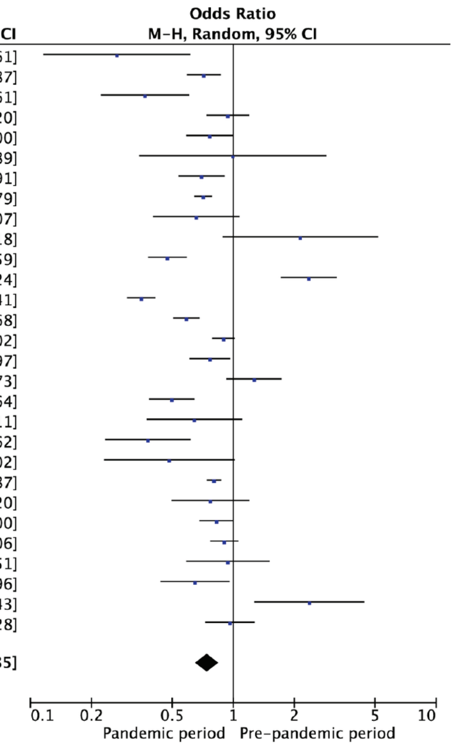

Figure 3. Forest plot of survival to hospital admission among OHCA patients in COVID-19 vs. pre-pandemic periods. The center of each square represents the standardized mean differences for individual trials, and the corresponding horizontal line stands for a 95% confidence interval. The diamonds represent pooled results

COVID-19: Coronavirus disease-2019, OHCA: Out-of-hospital cardiac arrest, CI: Confidence irterval

Study or Subgroup	Pandemic period Events	Pandemic period Total	Pre-pandemic period Events	Pre-pandemic period Total	Weight	Odds Ratio M-H, Random, 95% CI
Ahn 2021	7	152	15	145	2.4%	0.42 [0.17, 1.06]
Baert 2020	26	937	99	1546	4.6%	0.42 [0.27, 0.65]
Baldi 2020	16	490	21	321	3.4%	0.48 [0.25, 0.94]
Ball 2020	22	380	142	1218	4.5%	0.47 [0.29, 0.74]
Biskupski 2022	25	86	8	28	2.3%	1.02 [0.40, 2.63]
Chavez 2022	326	4418	360	3619	6.0%	0.72 [0.62, 0.84]
Cho 2020	8	171	14	158	2.5%	0.50 [0.21, 1.24]
Chugh 2022	90	907	201	1315	5.5%	0.61 [0.47, 0.80]
Fothergill 2021	49	1108	70	658	4.9%	0.39 [0.27, 0.57]
Leung 2023	19	2185	33	1502	3.9%	0.39 [0.22, 0.69]
Lim 2021 (B)	49	888	69	888	4.9%	0.69 [0.47, 1.01]
Lim 2022	34	1241	45	1118	4.5%	0.67 [0.43, 1.06]
Liu 2023	11	497	30	567	3.3%	0.41 [0.20, 0.82]
Marijon 2020	16	517	1614	8783	4.3%	0.14 [0.09, 0.23]
Morton 2022	16	181	11	147	2.8%	1.20 [0.54, 2.67]
Navalpotro-Pascual 2021	4	313	18	306	1.9%	0.21 [0.07, 0.62]
Ortiz 2020	108	1446	168	1723	5.6%	0.75 [0.58, 0.96]
Phattharapornjaroen 2022	2	60	8	76	1.1%	0.29 [0.06, 1.44]
Ristau 2022	475	1880	645	2289	6.0%	0.86 [0.75, 0.99]
Riyapan 2022	7	350	25	341	2.7%	0.26 [0.11, 0.60]
Sultanian 2021	17	1016	65	930	4.0%	0.23 [0.13, 0.39]
Sung 2022	134	1214	189	1605	5.7%	0.93 [0.73, 1.18]
Talikowska 2021	17	145	48	501	3.8%	1.25 [0.70, 2.25]
Uy-Evanado 2021	22	278	34	231	3.9%	0.50 [0.28, 0.88]
Yap 2022	2	221	6	274	1.1%	0.41 [0.08, 2.04]
Yu 2021	31	622	34	570	4.3%	0.83 [0.50, 1.36]
Total (95% CI)		**21703**		**30859**	**100.0%**	**0.54 [0.45, 0.65]**
Total events	1533		3972			

Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 118.72$, df = 25 ($P < 0.00001$); $I^2 = 79\%$
Test for overall effect: Z = 6.61 ($P < 0.00001$)

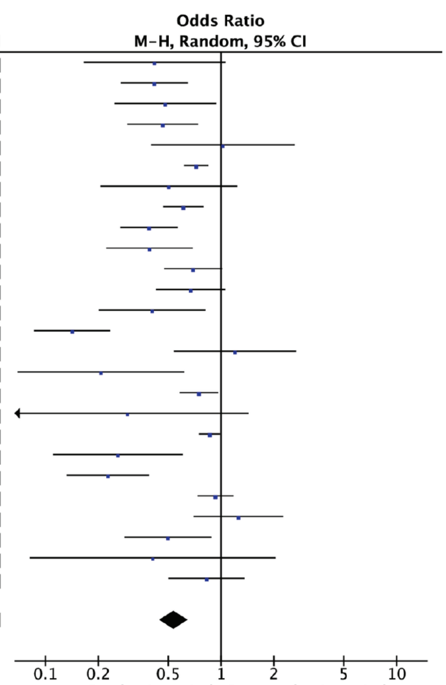

Figure 4. Forest plot of survival to hospital discharge among OHCA patients in COVID-19 vs. pre-pandemic periods. The center of each square represents the standardized mean differences for individual trials, and the corresponding horizontal line stands for a 95% CI. The diamonds represent pooled results

COVID-19: Coronavirus disease-2019, OHCA: Out-of-hospital cardiac arrest, CI: Confidence irterval

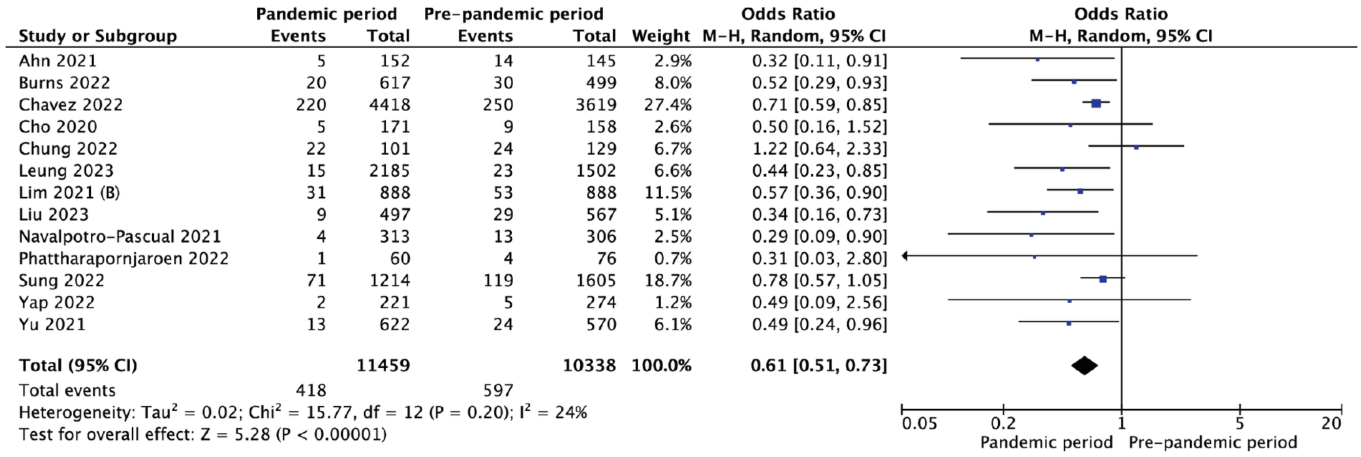

Figure 5. Forest plot of survival to hospital discharge with good neurological outcome among OHCA patients in COVID-19 vs. pre-pandemic periods. The center of each square represents the standardized mean differences for individual trials, and the corresponding horizontal line stands for a 95% CI. The diamonds represent pooled results

COVID-19: Coronavirus disease-2019, OHCA: Out-of-hospital cardiac arrest, CI: Confidence irterval

Table 2. Baseline patient characteristics among included trials

Outcome	Number of studies	Event/participants or mean±SD		Events		Heterogeneity between trials		p value for differences across groups
		COVID-19	Pre-pandemic	OR or MD	95% CI	p value	I^2 statistics	
Sex, male	34	37,557/64,776 (57.9%)	48,605/80,195 (60.6%)	1.01	0.97 to 1.05	0.05	30%	0.52
Age, years	32	69.4±15.1	68.6±16.3	-0.00	-0.56 to 0.56	<0.001	96%	1.00
Medical cause of CA	14	42,724/45,330 (94.3%)	29,032/31,037 (93.5%)	0.85	0.61 to 1.17	<0.001	94%	0.31
Home/nursing facility location in CA	25	49,334/56,008 (88.1%)	57,416/72,867 (78.8%)	1.41	1.24 to 1.61	<0.001	87%	**<0.001**
Witnessed status	22	10,771/19,865 (54.2%)	28,785/47,150 (61.0%)	1.12	0.95 to 1.32	<0.001	93%	0.18
Bystander witnessed	16	8,900/20,923 (42.5%)	8,753/19,218 (45.5%)	0.99	0.87 to 1.13	<0.001	85%	0.91
Witnessed by EMS	9	1,438/11,610 (12.4%)	1,376/11,602 (11.9%)	1.06	0.96 to 1.17	0.26	21%	0.28
Bystander CPR	28	12,979/59,507 (21.8%)	23,453/63,259 (37.1%)	1.03	0.91 to 1.17	<0.001	92%	0.64
Prehospital AED application	20	988/17,863 (5.5%)	1,550/27,270 (5.7%)	0.77	0.62 to 0.96	<0.001	78%	**0.02**
EMS arrival time	25	10.3±5.5	10.1±3.6	0.95	0.48 to 1.43	<0.001	100%	**<0.001**
On scene time	9	18.9±8.6	18.5±7.4	1.90	1.09 to 2.71	<0.001	99%	**<0.001**
The first defibrillation time	3	14.7±4.9	12.5±4.3	2.68	1.33 to 4.02	<0.001	99%	**<0.001**
Shockable rhythm	30	4,362/57,978 (7.5%)	9,645/70,254 (13.7%)	0.88	0.79 to 0.98	<0.001	75%	**0.02**
Adrenaline administration	13	6,981/12,534 (55.7%)	5,399/10,381 (52.0%)	1.13	0.87 to 1.48	<0.001	91%	0.36
Amiodarone administration	6	512/6,502 (7.9%)	532/4,819 (11.0%)	1.03	0.64 to 1.66	<0.001	91%	0.91
Atropine administration	2	23/862 (2.7%)	44/1,731 (2.5%)	1.55	0.43 to 5.56	0.05	73%	0.50
Defibrillation	7	1,549/34,935 (4.4%)	1,554/23,592 (6.6%)	0.91	0.83 to 1.01	0.24	25%	0.09
ACCD application	8	1,783/7,944 (22.4%)	1,646/8,841 (18.6%)	1.78	0.98 to 3.22	<0.001	97%	0.06
TTM application	5	96/2,709 (3.5%)	93/2,886 (3.2%)	0.64	0.30 to 1.34	0.02	65%	0.23

ACCD: Automated chest compression device, AED: Automated external defibrillator, CA: Cardiac arrest, CI: Confidence interval, CPR: Cardiopulmonary resuscitation, EMS: Emergency medicine service, MD: Mean difference, OR: Odds ratio, TTM: Targeted temperature management, SD: Standard deviation equipment, disinfection protocols, and screening procedures, can add extra time to the EMS response process (70). EMS providers must ensure their own safety and minimize the risk of virus transmission, which may contribute to increased on-scene time (71). The COVID-19 pandemic has prompted modifications in EMS protocols and procedures to adapt to the unique challenges posed by the virus (72,73). These changes may include additional screening questions, altered resuscitation techniques to minimize aerosol generation, and modifications in transport destinations. These adaptations and new protocols may require additional time, affecting both on-scene time and time to the first defibrillation. The overwhelming impact of the COVID-19 pandemic on healthcare systems has resulted in overcrowded hospitals, strained intensive care units, and limited resources. This strain on the healthcare system can lead to delays in transferring OHCA patients to the hospital, potentially prolonging on-scene time and delaying the initiation of definitive care.

The study also identified a statistically significant reduction in the incidence of shockable rhythms during the COVID-19 period. This finding raises concerns about delayed recognition of shockable rhythms or changes in the underlying etiology of OHCA cases during the pandemic. It is crucial to explore the reasons behind this reduction and consider potential strategies to ensure prompt recognition and appropriate treatment of shockable rhythms, as they are associated with better survival outcomes (74,75).

The study found a significant decrease in both survival to hospital admission and SHD rates during the COVID-19 period compared with the pre-pandemic period. These findings suggest that the COVID-19 pandemic has had a detrimental effect on the outcomes of OHCA patients.

One of the factors contributing to the lower survival rates is delayed access to healthcare facilities. The pandemic has put a strain on healthcare systems, with hospitals overwhelmed by the influx of COVID-19 patients (76). This increased demand for healthcare resources and personnel may lead to delays in receiving timely and appropriate care for OHCA patients. The strain on the healthcare system can result in longer wait times for ambulance transport, emergency department overcrowding, and limited availability of critical care resources, all of which can negatively impact survival rates (77).

Furthermore, the increased time intervals in the resuscitation process may also contribute to the lower survival rates observed during the COVID-19 period. Factors such as delayed recognition of cardiac arrest, prolonged EMS arrival time, and increased on-scene time have been reported during the pandemic (78). These delays can result from various reasons, including the need for additional infection control measures, altered EMS protocols, and increased demands on EMS providers. The prolonged resuscitation process may lead to delayed initiation of interventions such as CPR, defibrillation, and the administration of medications, which are crucial for improving survival outcomes in OHCA cases.

Changes in the availability of resources and personnel can also impact OHCA outcomes during the COVID-19 period. The pandemic has led to the reassignment of healthcare workers to COVID-19-related duties, reduced availability of certain medical supplies and equipment, and limitations on healthcare personnel due to illness or quarantine measures (79). These factors may affect the overall quality and effectiveness of resuscitation efforts, potentially leading to poorer outcomes for OHCA patients.

Furthermore, the analysis of SHD with a good neurological outcome showed a lower proportion of favorable outcomes during the COVID-19 period compared with the pre-pandemic period. This suggests that not only are survival rates affected but the quality of survival in terms of neurological function is also compromised. The reasons for this decline in neurological outcomes may be multifactorial, including delays in resuscitation, limited access to specialized care, and potential disruptions in post-resuscitation management during the pandemic.

Moreover, according to emerging research, COVID-19 can cause a hypercoagulable state, resulting in the production of minute blood clots or microthrombi throughout the body (80). This microthrombi has the potential to alter blood flow, notably in the coronary arteries, increasing the risk of cardiac events such as OHCA (81,82). The inflammatory response of the virus and the direct damage it causes to the blood vessel endothelium aggravate this prothrombotic environment (83-85). As a result, the greater incidence of OHCA reported in COVID-19 patients may be attributable to part to the disease's elevated risk of microthrombosis.

Study Limitations

The study presented here is not without limitations. One limitation is the heterogeneity in the number of patients in each study. Another limitation of the study that may affect the results is population diversity.

Conclusion

COVID-19, compared with the pre-pandemic period, was characterized by a reduced rate of defibrillation rhythms during OHCA, as well as a worse prognosis in terms of both survival to hospital admission, SHD, and SHD good neurological outcome.

Ethics

Ethics Committee Approval and Informed Consent: Not applicable due to the character of study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.D., Design: M.D., Data Collection or Processing: M.D., M.P., L.S., Analysis or Interpretation: M.D., B.C., N.B., L.S., Literature Search: M.D., M.P., L.S., Writing: M.D., D.S., M.P., B.C., M.G., N.B., L.S.

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