RESUSCITATION 194 (2024) 110043

Available online at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

The impact of COVID-19 pandemic on out-of-hospital cardiac arrest: An individual patient data meta-analysis

Enrico Baldi[a,b,*], *Catherine Klersy*[c], *Paul Chan*[d], *Jonathan Elmer*[e], *Jocasta Ball*[f,g,h], *Catherine R. Counts*[i,j], *Fernando Rosell Ortiz*[k], *Rachael Fothergill*[l], *Angelo Auricchio*[m,n,o], *Andrea Paoli*[p], *Nicole Karam*[q], *Bryan McNally*[r], *Christian Martin-Gill*[e], *Ziad Nehme*[f,h], *Christopher J. Drucker*[s], *José Ignacio Ruiz Azpiazu*[k], *Adam Mellett-Smith*[l], *Ruggero Cresta*[m,t], *Tommaso Scquizzato*[u], *Xavier Jouven*[q], *Roberto Primi*[a,b], *Rabab Al-Araji*[v], *Francis X. Guyette*[e], *Michael R. Sayre*[i,j], *Antonio Daponte Codina*[w], *Claudio Benvenuti*[m], *Eloi Marijon*[q], *Simone Savastano*[a,b], *the OHCA-COVID study group*

Abstract

Aim: Prior studies have reported increased out-of-hospital cardiac arrests (OHCA) incidence and lower survival during the COVID-19 pandemic. We evaluated how the COVID-19 pandemic affected OHCA incidence, bystander CPR rate and patients' outcomes, accounting for regional COVID-19 incidence and OHCA characteristics.

Methods: Individual patient data meta-analysis of studies which provided a comparison of OHCA incidence during the first pandemic wave (COVID-period) with a reference period of the previous year(s) (pre-COVID period). We computed COVID-19 incidence per 100,000 inhabitants in each of 97 regions per each week and divided it into its quartiles.

Results: We considered a total of 49,882 patients in 10 studies. OHCA incidence increased significantly compared to previous years in regions where weekly COVID-19 incidence was in the fourth quartile (>136/100,000/week), and patients in these regions had a lower odds of bystander CPR (OR 0.49, 95%CI 0.29–0.81, p = 0.005). Overall, the COVID-period was associated with an increase in medical etiology (89.2% vs 87.5%, p < 0.001) and OHCAs at home (74.7% vs 67.4%, p < 0.001), and a decrease in shockable initial rhythm (16.5% vs 20.3%, p < 0.001). The COVID-period was independently associated with pre-hospital death (OR 1.73, 95%CI 1.55–1.93, p < 0.001) and negatively associated with survival to hospital admission (OR 0.68, 95%CI 0.64–0.72, p < 0.001) and survival to discharge (OR 0.50, 95%CI 0.46–0.54, p < 0.001).

Conclusions: During the first COVID-19 pandemic wave, there was higher OHCA incidence and lower bystander CPR rate in regions with a high-burden of COVID-19. COVID-19 was also associated with a change in patient characteristics and lower survival independently of COVID-19 incidence in the region where OHCA occurred.

Keywords: Out-of-hospital cardiac arrest, COVID-19, SARS-CoV-2, Individual patient data meta-analysis

* Corresponding author at: Division of Cardiology Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.
E-mail address: enrico.baldi@unipv.it (E. Baldi).

https://doi.org/10.1016/j.resuscitation.2023.110043
Received 30 August 2023; Received in Revised form 4 November 2023; Accepted 6 November 2023

0300-9572/

Background

Out-of-hospital cardiac arrest (OHCA) is a major health issue with a survival rate of between 4.6%–16.4% depending on the region.[1,2] After SARS-CoV-2 emergence,[3,4] the World Health Organization declared the "Coronavirus disease 2019" (COVID-19) pandemic on 11st March 2020.[5] Many countries reported a major increase in OHCA during the first pandemic wave compared to the same period in previous years,[6–13] although this was not seen everywhere.[14–23] A potential relationship between COVID-19 pandemic waves and an increase in OHCA incidence was reported,[24,25] but data are limited. Moreover, COVID-19 has the capacity to affect the chain of survival (i.e. actions to be implemented, from the community response to in-hospital treatment, to increase OHCA survival)[26] particularly as it relates to bystander cardiopulmonary resuscitation (CPR), with a number of studies reporting a decrease in its occurrence during the pandemic,[6-10,17,22,27] whilst some saw no change[11,16,18–20] and others even an increase[15,28]. A change in witnessed status and in OHCA location was also highlighted,[6,7,9,15] likely a result of quarantines and social distancing. A dramatic reduction in various outcome measures were reported regardless of COVID-19 incidence during the first wave in most regions.[9,10,11,15,21,28,29] To date, only data at a regional/country-level or aggregated meta-analyses have been published. An individual patient data (IPD) meta-analysis[30] is therefore useful to further investigate the relationship between OHCA and COVID-19, especially during the first wave, when the world was unprepared, thus enabling better readiness in case of future pandemics.

The aim of this study was to assess how the first COVID-19 pandemic wave in 2020 affected OHCA incidence, therefore the OHCA incidence was modelled accounting for the background regional COVID-19 incidence. Moreover, we evaluated also how COVID-19 pandemic affected bystander CPR rate and OHCA patients' outcome.

Methods

This is an IPD meta-analysis coordinated by the Fondazione IRCCS Policlinico San Matteo (Pavia,Italy). The reporting of this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Individual Patient Data (PRISMA-IPD) guidelines[31] and the protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021275184).

Eligibility criteria

The study question was framed using the Population, Intervention, Comparison, Outcome (PICO) format. The two PICOs were "Among adults, did the COVID-19 pandemic compared to the pre-pandemic period, affect OHCA incidence?" and "Among adult OHCA patients, did the COVID-19 pandemic compared to the pre-pandemic period affect the bystander CPR rate and OHCA patients' outcome?".

We considered the following endpoints: bystander CPR, pre-hospital death (i.e. death before the initiation of patient transport to hospital), survival to hospital admission (i.e. patient in whom a ROSC was sustained until arrival at the emergency department and transfer of care to medical staff at the receiving hospital - corresponding to the Utstein recommendations' core outcome "Survived event"[32]) and survival to hospital discharge (or at 30-days).

We included data from published observational studies. Only those studies providing a comparison of the OHCA incidence during the first pandemic wave (COVID-period) with a reference period of the previous year(s) (pre-COVID period) and indicating the bystander CPR rate, the witnessed status, and the OHCA location were considered.

The study included only subjects already considered in the published papers, both for the 2020 period and for the comparison one (s).

All languages were included if there was an English abstract.

Information sources, search strategy and study selection

On 1st February 2021, we searched PubMed and Embase for original studies published before 31st December 2020 regarding OHCA during COVID-19 (query search in Appendix1).

Two reviewers (EB, RP) independently screened all titles and abstracts retrieved from the systematic search, then independently reviewed the full texts of all potentially relevant publications passing the first level of screening. In case of disagreement, a third reviewer (SS) was included as a tiebreaker.

Data extraction

Once eligible publications were identified, the corresponding research groups were asked to participate via e-mail. If they did not respond to an initial inquiry, one follow-up email was sent approximately 2 weeks later.

Those groups that agreed to participate provided a dataset (Appendix2) following Utstein-style 2014.[32] All the registries participating in this study have been approved by ethics committees, if required, and appropriate data transfer agreements have been realised.

Risk of bias assessment

We used the Newcastle-Ottawa quality assessment scale to assess the methodological quality for the included cohort studies.[33]

Statistical analysis

We performed analyses using Stata, rel.17 (StataCorp, College Station, USA). A 2-sided p-value < 0.05 was considered statistically significant. For post-hoc comparisons, the Bonferroni correction for significance level was applied. Data are described, based on an assessment of normality, with the mean and standard deviation or the median and interquartile range if continuous and as counts and percent if categorical, overall, by cohort and by bystander CPR.

According to Utstein recommendations,[32] we considered all the patients for analysing the effect of COVID-19 incidence on OHCA rate and only the patients in whom CPR was started by EMS for the other analyses.

We computed the weekly COVID-19 incidence (Monday-to-Sunday) per 100,000 inhabitants in each region for 2020. A total of 97 regions were analysed: five in Italy, one in Australia, one in England, 51 in the U.S., 10 in Spain, 25 in Switzerland and four in France. The COVID-19 incidence was divided into quartiles and their association with OHCA counts were modelled using negative binomial regression. Incidence rate ratios with respect to the lowest quartile were computed together with their 95% confidence intervals

(95%CI). The analyses were adjusted for the number of OHCAs in the preceding year and the week when the OHCA occurred. Huber-White robust standard errors were computed to account for intra-study correlation.

Multivariable logistic models including a set of predefined candidate predictors of the different endpoints were fitted, while computing Huber-White robust standard errors to account for intra-study correlation. Predictors were type of cohort (Pre-COVID/COVID), age, sex, medical etiology, bystander witnessed, public place, bystander CPR, shockable rhythm, quartiles of incidence of COVID-19, and pre-hospital death. Odds ratios (OR) and 95%CI were estimated from the models. The model area under the receiver operating characteristic curve (AUC-ROC) was computed to assess model discrimination.

Results

The results of literature search are described in the PRISMA flow diagram (Fig. 1): a total of 82 studies were found via the search criteria and via manual search, 64 were excluded. No disagreement was identified between the two reviewers. Consequently, the patient level data was requested from 18 research groups (Supplementary Tab.1) and was provided from 10. Across the 10 studies, 49,882 patients were included, 28,213 in pre-COVID period and 21,669 in COVID period. The distribution of patients among the studies is presented in Supplementary Tab.2. The risk of bias, according to the Newcastle-Ottawa scale, was considered low for all 10 studies considering that all the data come from existing OHCA registries which enrol all the consecutive cases of OHCAs in a region, the method

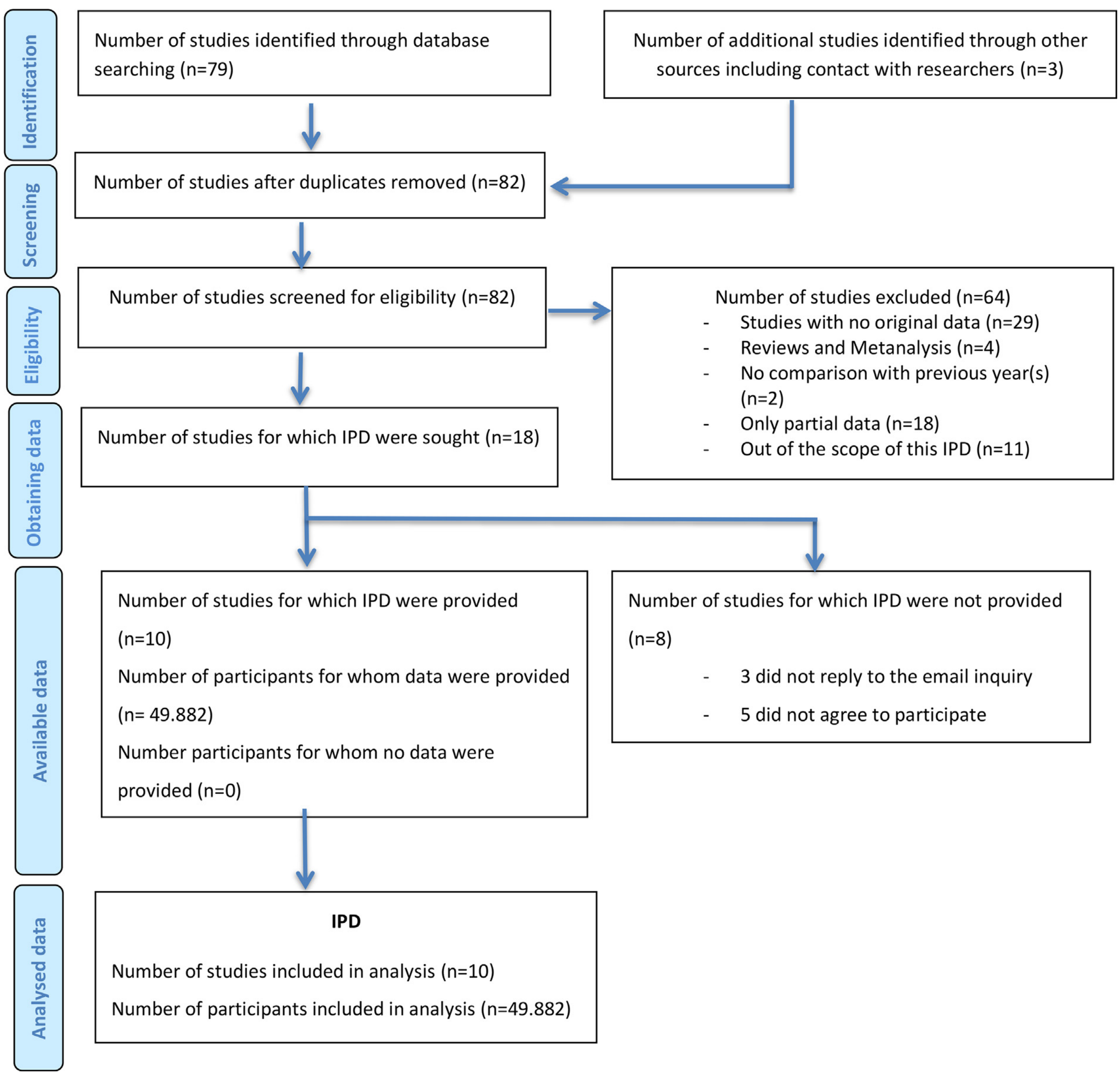

Fig. 1 – PRISMA IPD Flow Diagram.

Table 1 – Negative binomial regression regarding change in OHCA rate considering the quartile of COVID-19 incidence.

Model Wald Chi2(5) 95.18, model p < 0.001

	IRR (95%CI)	p-value
Quartiles of incidence of COVID-19		<0.001
≤ 6	1.0	
6 – 32	1.19 (0.79 – 1.8)	0.4
32 – 136	1.71 (0.95 – 3.07)	0.07
> 136	2.41 (1.32 – 4.40)	0.004
preOHCA	1.02 (1.01–1.02)	<0.001
Week	1.00 (0.98–1.02)	0.876

Post-hoc comparisons; p for significance p<0.008

	IRR (95%CI)	p-value
Quartiles of incidence of COVID-19		
6–32 vs ≤ 6	1.19 (0.79–1.80)	0.4
32–136 vs ≤ 6	1.71 (0.95–3.07)	0.07
> 136 vs ≤ 6	2.41 (1.32–4.40)	0.004
32–136 vs 6–32	1.43 (1.14–1.80)	0.002
> 136 vs 6–32	2.02 (1.41–2.89)	<0.001
> 136 vs 32–136	1.41 (1.06–1.87)	0.017

IRRs (incidence rate ration) express by how much the count in the low incidence quartile is multiplied in the other quartiles.

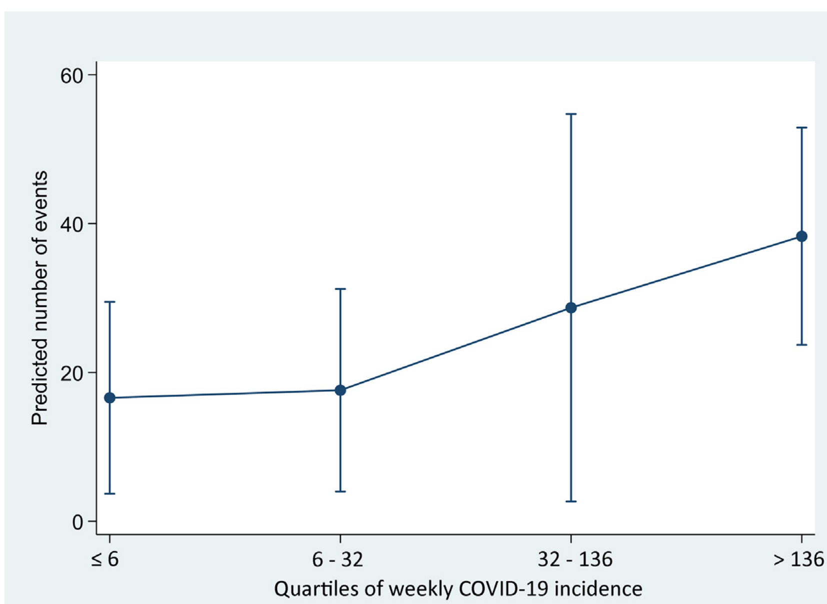

Fig. 2 – Number of OHCA events stratifies by quartiles of OHCA incidence (Unadjusted negative binomial regression).

of enrolling OHCAs patients was unchanged before and during the pandemic and that the controls are the patients with the same criteria (suffering OHCA) before the outbreak.

OHCA and COVID-19 incidence

The negative binomial regression evaluating the change in OHCA counts accordingly to the COVID-19 incidence for each region in each week of the year shown in Table 1 and Fig. 2 highlights that the number of OHCA significantly increased compared to the previous years in regions in which the weekly COVID-19 incidence was in the fourth quartile (higher than 136/100,000/week).

Patients' characteristics

Comparing patients' and OHCAs' characteristics in pre-COVID and COVID period, an increase in medical etiology (87.5% vs 89.2%, p < 0.001) and home as OHCA location (67.4% vs 74.7%, p < 0.001) was seen, as well as a decrease in shockable initial rhythm (20.3% vs 16.5%,p < 0.001), survival to hospital admission

Table 2 – Comparison between patients' and OHCAs' characteristics in COVID and pre-COVID period.

Variable	*Pre-COVID (n = 18434)*	*COVID (n = 16703)*	*p*
Males, n (%)	11,688 (63.4)	10,329 (61.8)	<0.01
Age, years [IQR]			0.44
≤ 54	5015 (27.2)	4392 (26.5)	
54–67	4964 (26.9)	4524 (27.3)	
67 – 79	4675 (25.4)	4202 (25.4)	
>79	3754 (20.4)	3439 (20.8)	
Etiology of arrest, n (%)			<0.01
Medical	16,125 (87.5)	14,893 (89.2)	
Trauma	332 (1.8)	204 (1.2)	
Drowning	98 (0.5)	60 (0.4)	
Overdose	850 (4.6)	811 (4.9)	
Electrocution	16 (0.1)	7 (0.1)	
Asphyxial (external causes)	271 (1.5)	249 (1.5)	
Unknown	742 (4.0)	479 (2.9)	
Country			<0.001
Australia	1359 (7.4)	450 (2.7)	
England	658 (3.6)	1135 (6.8)	
Italy	420 (2.3)	493 (2.9)	
Spain	1600 (8.7)	1443 (8.6)	
Switzerland	527 (2.9)	564 (3.4)	
USA	13,870 (75.2)	12,618 (75.5)	
OHCA location, n (%)			<0.001
Home	12,436 (67.4)	12,485 (74.7)	
Nursing residence	1763 (9.6)	1731 (10.4)	
Workplace	181 (1.0)	71 (0.4)	
Educational	4 (0.02)	1 (0.01)	
Street	1352 (7.3)	944 (5.6)	
Public building	1649 (8.9)	956 (5.7)	
Sport	209 (1.1)	81 (0.5)	
Other	284 (1.5)	270 (1.6)	
Unknown	556 (3.0)	164 (1.0)	
Witnessed status, n (%)			<0.001
Bystander witnessed	7998 (43.4)	6888 (41.2)	
Unwitnessed	8131 (44.1)	7636 (45.7)	
Witnessed by EMS	2114 (11.5)	2108 (12.6)	
Unknown	191 (1.04)	71 (0.4)	
Bystander CPR, n (%) [†]	8663 (53.8)	7482 (52.1)	<0.01
AED connected, n (%)			<0.001
Yes	5323 (28.9)	4471 (26.8)	
No	12,865 (69.8)	11,962 (71.6)	
Initial rhythm, n (%) [‡]			<0.001
Shockable	3549 (20.3)	2699 (16.5)	
Not shockable	13,943 (79.7)	13,643 (83.5)	
Mechanical CPR, n (%) [¶]			<0.001
Yes	3833 (24.7)	4023 (27)	
No	9574 (61.6)	8359 (56.1)	
Unknown	2125 (13.7)	2529 (17)	
Outcome, n (%) [‡]			<0.001
Pre-hospital death	7754 (42)	8945 (53.6)	
Transported with ROSC	4791 (26)	3238 (19.4)	
Transported with ongoing CPR	5879 (31.9)	4495 (26.9)	
Unknown	10 (0.1)	25 (0.1)	
Survival to hospital admission, n (%)			<0.001
Yes	5810 (31.5)	3812 (22.8)	
No	11,599 (62.9)	11,517 (69)	
Unknown	1025 (5.6)	1374 (8.2)	

(*continued on next page*)

Table 2 (continued)

Variable	*Pre-COVID (n = 18434)*	*COVID (n = 16703)*	*p*
Survived to hospital discharge, n (%) ‡			<0.001
Yes	1761 (9.6)	732 (4.4)	
No	14,755 (80)	13,335 (79.8)	
Unknown	1918 (10.4)	2636 (15.8)	

Mann–Whitney U test was used for comparison of continuous variables and Chi-square test was used for comparison of categorical variables.

EMS: emergency medical service; OHCA: out-of-hospital cardiac arrest; CPR: cardio-pulmonary resuscitation; ACLS: advanced cardiac life support (i.e. endotracheal intubation, administration of drugs, mechanical CPR); ROSC: return of spontaneous circulation.

† Among those in whom resuscitation was attempted by EMS and excluding those witnessed by EMS.

‡ Among those in whom resuscitation was attempted by EMS.

¶ Among those in whom ACLS was initiated.

Table 3 – Multivariable logistic regression model for the probability of receiving bystander CPR. Area under ROC curve = 0.56.

Candidate predictors	OR (95%CI)	p
Cohort		
PreCOVID	1.0	
COVID	1.09 (0.96–1.23)	0.17
Age Group		0.52
≤ 54	1.0	
55–67	0.99 (0.89–1.09)	0.79
68 – 79	1.07 (0.98–1.18)	0.12
> 79	1.07 (0.88–1.31)	0.50
Sex		
Female	1.0	
Male	0.93 (0.85–1.00)	0.06
Medical etiology		
No	1.0	
Yes	1.16 (0.8–1.70)	0.43
Bystander witnessed		
No	1.0	
Yes	1.28 (0.99–1.67)	0.06
Public		
No	1.0	
Yes	2.27 (1.25–4.14)	0.007
Quartiles of incidence of COVID-19		<0.001
≤ 6	1.0	
6 – 32	0.73 (0.45–1.19)	0.21
32 – 132	0.64 (0.38–1.12)	0.12
> 136	0.49 (0.29–0.81)	0.005

Bonferroni correction has to be considered if the candidate predictor has more than two categories: the statistically significant p-value is less than 0.025 if there are three categories and is less than 0.017 if there are four categories for the shown comparisons against the reference category.

(31.5% vs 22.8%,p < 0.001) and survival to hospital discharge (9.6% vs 4.4%,p < 0.001) (Table 2). The comparison among patients' characteristics according to the different quartiles of COVID-19 incidence in the COVID period is presented in Supplementary Tab. 3.

Percentage of bystander CPR

We found that the OHCA occurrence in a public location was positively associated with the probability of receiving bystander CPR (OR 2.27, 95%CI 1.25–4.14,p = 0.007), whilst the OHCA occurrence in a region with a weekly COVID-19 incidence in the fourth quartile was negatively associated with that (OR 0.49, 95%CI 0.29–0.81,p = 0.005) (Table 3). These associations were not confirmed restricting the analysis to patients in the Utstein Comparator Group (i.e. bystander witnessed and a shockable initial rhythm). (Supplementary Tab.4).

Survival outcomes

The multivariable logistic regression model demonstrated that OHCAs occurring during the COVID period were associated with an increased likelihood of pre-hospital death (OR 1.73, 95%CI 1.55–1.93,p < 0.001). Other predictors of increased likelihood of pre-hospital death included older age groups, male gender and medical etiology. The different quartiles of incidence of COVID-19 were not associated with pre-hospital death, while public location and shockable initial rhythm were negatively associated with this outcome (Supplementary Tab.5).

Concerning survival to hospital admission, older age groups, male gender, medical etiology, bystander CPR and the COVID period (OR 0.68, 95%CI 0.64–0.72,p < 0.001) were negatively associated with this outcome. The different quartiles of incidence of COVID-19 were not associated with survival to hospital admission, whilst witnessed events, a public location and a shockable initial rhythm were positively associated with that (Table 4). The adjusted survival to hospital admission comparing pre-COVID and COVID period within quartiles of COVID-19 incidence is presented in Supplementary Fig. 1.

The COVID period was negatively associated with survival to hospital discharge (OR 0.50, 95%CI 0.46–0.54,p < 0.001). Moreover, older age groups and medical etiology were inversely associated with survival to hospital discharge, whilst witnessed events, a public location and a shockable initial rhythm were positively associated with survival to hospital discharge. No associations were observed for gender or bystander CPR (Supplementary Tab.6).

Discussion

This study is the first IPD meta-analysis designed to specifically evaluate the global impact of the first COVID-19 pandemic wave on OHCA incidence, patients' characteristics, and survival outcomes. The main results of our study, which included 49,882 patients from 10 different studies in 97 regions, six countries and three continents,

Table 4 – Multivariable logistic regression model for the probability of surviving to hospital admission Area under ROC curve = 0.71.

Candidate predictors	OR (95%CI)	p
Cohort		
PreCOVID	1.0	
COVID	0.68 (0.64–0.72)	<0.001
Age Group		<0.001
≤ 54	1.0	
55–67	0.89 (0.85–0.94)	<0.001
68 – 79	0.75 (0.71–0.80)	<0.001
> 79	0.57 (0.49–0.67)	<0.001
Sex		
Female	1.0	
Male	0.78 (0.75–0.81)	<0.001
Medical etiology		
No	1.0	
Yes	0.54 (0.46–0.63)	<0.001
Bystander witnessed		<0.001
None		
Bystander	2.40 (2.01–2.86)	<0.001
EMS	3.67 (3.32–4.07)	<0.001
Public		
No	1.0	
Yes	1.37 (1.20–1.57)	<0.001
Bystander CPR		
No	1.0	
Yes	0.93 (0.87–0.99)	0.02
Shockable rhythm		
No	1.0	
Yes	2.74 (2.17–3.47)	<0.001
Quartiles of incidence of COVID-19		<0.01
≤ 6	1.0	
6 – 32	1.08 (0.93–1.25)	0.31
32 – 136	0.99 (0.81–1.21)	0.92
> 136	1.08 (0.96–1.21)	0.18

Bonferroni correction has to be considered if the candidate predictor has more than two categories: the statistically significant p-value is less than 0.025 if there are three categories and is less than 0.017 if there are four categories for the shown comparisons against the reference category.

were: 1)the rate of OHCA during COVID-19 pandemic significantly increased in regions with a high burden of COVID-19 infections (>136/100,000/week); 2)an increase of OHCAs with medical etiology and occurring at home as well as a decrease in shockable initial rhythm was found during COVID period; 3)the occurrence of OHCA in a region with a weekly COVID-19 incidence in the fourth quartile was negatively associated with bystander CPR; 4)a decrease in the percentage of patients who survived until hospital admission was highlighted independently by the COVID-19 incidence of the region where the OHCA occurred.

Results from previous studies have shown a significant variability concerning the increase in OHCA incidence in different countries during the first pandemic. A dramatic surge in OHCA was highlighted in the Lombardy region in Italy,[6] in Paris area,[9] in some areas of England,[28,34] U.S.,[11,21] Canada[35] and in Brazil.[36] On the contrary in other areas of the same previously reported countries such as the Padua[20] and Bologna[19] areas in Italy, certain regions in the U. S.[10,16,18] and in other continents like Asia[37,38] and Australia,[39] the OHCA incidence during the first pandemic wave was similar compared to the same period of the previous years. The different burden of COVID-19 infection in different areas was considered as a possible explanation of this regional difference: a higher OHCA incidence in regions with a high county-level of COVID-19 mortality rate was outlined in the U.S.,[21] whilst a correlation between OHCA and COVID-19 incidence was highlighted in Lombardy Region.[24] However, these data are limited in number and areas and, moreover, are difficult to compare given the different indicators used to estimate the effect of COVID at local level. We chose to use the COVID-19 incidence per 100,000 inhabitants in each region where the patient had the OHCA in the week when the OHCA occurred to better explore the impact of COVID-19 infection. Therefore, using the negative binomial regression evaluating the change in OHCA counts accordingly to the COVID-19 incidence for each region in each week of the year, we were able to demonstrate that the OHCA rate significantly increased only in regions in which the weekly COVID-19 incidence was in the fourth quartile (>136/100,000/week), compared to the previous years.

This result confirms the preliminary evidence highlighted above and represent a practical finding of non-negligible importance as may help governments and healthcare politics, in case of future pandemics,[40] to identify territories with a higher risk of increased OHCAs through contagion trend monitoring. The reasons behind this increase in the regions highly burdened by COVID-19 may be multiple: direct virus' effect, as the increase of cardiovascular and respiratory causes leading to OHCA directly linked to SARS-CoV-2 infection[41,42]; indirect pandemic effect, as the fear of patients to in-hospital contagion which prevented them to activate the EMS, probably more common in the areas most affected by the pandemic,[43,44] and the burden on EMS system.[7,45] Therefore, in circumstances such as this, decision-makers should consider the reallocation of EMS resources and perform awareness campaign to stimulate the citizens to call EMS in case of symptoms suspected for a time-dependent disease at least in those regions where a weekly increase in pandemic incidence is observed.

Our study also confirmed that in many regions, in very different and distant geographical areas, during the COVID period there was an increase in OHCAs due to medical etiology and in OHCAs occurring at home. This latter evidence is easily explained by the numerous "lockdowns" implemented worldwide,[46] the former is probably due both to the direct effect of the SARS-CoV-2 infection outlined above and the relative reduction of other OHCAs causes, as trauma, which are typical of the social life inhibited during pandemic.[47] Also a decrease in shockable rhythm was confirmed in COVID period, and the reason may reside both in the increase of respiratory failure and the resulting hypoxia as the cause of OHCA due to SARS-CoV-2 infection[48] and in the increase of EMS arrival time which was outlined in some settings and which was also due to the time needed to wear personal protective equipment by EMS personnel.[7,10,49]

Concerning bystander CPR, the OHCA occurrence in public locations during the COVID period was associated with an increase in the percentage of bystander CPR, but it was highlighted that the percentage of bystander CPR was reduced by about 50% in the regions with a weekly COVID-19 incidence in the fourth quartile. Conversely, if the level of weekly COVID-19 incidence was lower than the threshold of 136/100,000/week, the association with the level of COVID-19 incidence and the difference in percentage of bystander CPR compared to the previous year was not confirmed. This association was not confirmed also restricting the analysis to the Utstein Comparator Group. The reason behind this evidence could be sought in the fear of bystander to perform CPR,[50] especially concerning mouth-to mouth ventilation,[51] which was already present before the pandemic and which could have been exacerbated by the peculiar transmission of SARS-CoV-2. The absence of an association between COVID-19 incidence and bystander CPR rate in the Utstein Comparator Group, could reside in the presence of someone who witnessed the event, most probably at home, given the lockdown. If bystanders witness the event, they are more willing to start CPR rather than if they find the patient already in cardiac arrest.[52] A recent meta-analysis had demonstrated that lockdown did not influenced the bystander willingness to perform CPR.[53] However, the difference compared to regions with high-incidence of COVID-19 in our study may be explained considering that they included the entire 2020 year, including OHCAs occurred after the end of the first pandemic peak, used aggregated data and did not evaluate the COVID-19 incidence in each region.[53]

Even more alarming than the increase of OHCA incidence and the decrease of bystander CPR is the dramatic worsening of patients' outcome. Indeed, on one hand, the common predictors of better outcome (i.e. younger age, female gender, non-medical etiology, public location and shockable initial rhythm)[54] were confirmed also during pandemic. However, on the other hand, it was highlighted that the OHCA occurrence during the COVID period was associated with worse outcome independently of the previous predictors and independently of the COVID-19 incidence in the region where the OHCA occurred. The percentage of patients who died before transport to the hospital increased by 73% and the percentage of patients who survived to hospital admission and to hospital discharge decreased by 32% and 50% respectively.

Our data regarding outcome confirm, on a wide population of OHCA patients from different countries with great difference in COVID-19 incidence, that also in regions only marginally affected by the pandemic the survival after OHCA dramatically decreased[39] and highlighted that this was independent of known predictors of outcome. The reasons behind this evidence are not completely clear and, accordingly to preliminary evidence, EMS response time and prehospital on-scene management may have an important role.[55] Future studies focused on this aspect are needed to avoid that the COVID-19 pandemic continues to negatively impact the outcome of OHCA patients lasts for a long time.[56] Moreover, our results may provide important evidence for global planning to improve the preparedness of community and health-care system in case of future pandemics.

Limitations

Our study has limitations. Firstly, not all the studies published about this topic in the selected timeframe agreed to join. However, this is the first IPD meta-analysis published so far on this topic, overcoming the limitations of studies coming from a single region/country. Secondly, we focused only on the first pandemic wave, which, however, represents the moment when the world was unprepared, thus enabling better readiness in case of future pandemics. Furthermore, more comprehensive IPD metanalysis may refine the results of our manuscript. Moreover, some evidence highlighted an increase in OHCA occurrence also during the other pandemic waves, therefore it is reasonable to believe that our results may also apply to other pandemic waves.[24]

Conclusions

The first COVID-19 pandemic wave in 2020 had a strong impact on OHCA, increasing the OHCA incidence in regions with a high-burden of COVID-19 infections, decreasing the bystander CPR rate. Moreover, a decrease in the rate of survival to hospital admission was demonstrated independently by the COVID-19 incidence of the region where the OHCA occurred.

Conflict of interest

E.B., C.K., J.B, C.R.C., F.R.O, R.F., A.A., A.P., E.M., B.M, Z.N., C.J. D., J.I.R.A., A.M., R.C., X.J., R.P., R.A., M.R.S, A.D.C., C.B., N.K., S.S. have no conflict of interest to declare. P.C. received funding from the National Heart Lung Blood Institute (grant award no. R01HL160734) and the American Heart Association unrelated to this study. J.E received National Institutes of Health grant funding unrelated to this study and is part of the Editorial Board of Resuscitation. T.S. is Social Media Editor of Resuscitation and Resuscitation Plus. F.X.G. received U.S. Department of Defense funding unrelated to this study. C.M. received grants from U.S. Department of Defense, National Institutes of Health, Kaiser Foundation/Gordon and Betty Moore Foundation and AASM Foundation, unrelated to this study.

Funding

No specific funding was obtained for the present study.

CRediT authorship contribution statement

Enrico Baldi: . **Catherine Klersy:** Writing – review & editing, Investigation, Data curation. **Paul Chan:** Writing – review & editing, Investigation. **Jonathan Elmer:** Writing – review & editing, Investigation. **Jocasta Ball:** Writing – review & editing, Investigation. **Catherine R Counts:** Writing – review & editing, Investigation, Data curation. **Fernando Rosell Ortiz:** Writing – review & editing, Investigation, Data curation. **Rachael Fothergill:** Writing – review & editing, Investigation. **Angelo Auricchio:** Investigation. **Andrea Paoli:** Investigation, Data curation. **Nicole Karam:** Investigation. **Bryan McNally:** Writing – review & editing, Investigation. **Christian Martin-Gill:** Investigation. **Ziad Nehme:** Investigation. **Christopher J. Drucker:** Investigation. **José Ignacio Ruiz Azpiazu:** Investigation. **Adam Mellett-Smith:** Investigation. **Ruggero Cresta:** Investigation, Data curation. **Tommaso Scquizzato:** Investigation. **Xavier Jouven:** Investigation. **Roberto Primi:** Investigation, Data curation. **Rabab Al-Araji:** Investigation, Data curation. **Francis X. Guyette:** Investigation. **Michael R. Sayre:** Investigation. **Antonio Daponte Codina:** Investigation. **Claudio Benvenuti:** Investigation. **Eloi Marijon:** Writing – review & editing, Investigation. **Simone Savastano:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

E.B., S.S. are part of the ESCAPE-NET consortium. E.B., S.S. are member of the European Resuscitation Council (ERC) Research-NET. This article is based upon work from COST Action PARQ CA19137, supported by COST (European Cooperation in Science and Technology).

"OHCA-COVID study group" researchers: Thomas D. Rea (University of Washington School of Medicine, Seattle, U.S.A.; King County Emergency Medical Services, Seattle, U.S.A.), Maria Luce Caputo (Fondazione Ticino Cuore, Lugano, Switzerland; Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, Lugano, Switzerland), Roman Burkart (Interverband für Rettungswesen IVR-IAS, Aarau, Switzerland), Luis Olavarria Gobantes (Centro de Emergencias 061 - Málaga, Spain), María José Luque-Hernández (Centro de Emergencias 061 - Málaga, Spain), Miguel Angel Paz Rodríguez (Centro de Emergencias 061 - Huelva, Spain), Fernando Ayuso Batista (Centro de Emergencias 061 - Córdoba, Spain), Carmen Gutiérrez-García (Centro de Emergencias 061 - Málaga, Spain), María Remedios Soto-García (Centro de Emergencias 061 - Málaga, Spain), María Auxiliadora Caballero-García (Centro de Emergencias 061 - Sevilla, Spain), Belen Mainar (Servicio de Emergencias 061 - Aragon, Spain), Sonia Royo Embid (Servicio de Emergencias 061 - Aragon, Spain), Roberto Antón Ramas (Servicio de Emergencias 061 - Aragon, Spain), Marcel Chueca García (Servicio de Emergencias 061 - Aragon, Spain), Ignacio González Herráiz (Servicio de Emergencias 061 - Aragon, Spain), Maria Isabel Ceniceros Rozalen (SAMU061-IB-SALUT, Palma, Spain), Esther Arias Moya (SAMU061-IB-SALUT, Palma, Spain), María Noemí Gonzalez Quintana (Servcio de Urgencias Canario (SUC), Las Palmas de Gran Canaria, Spain), Faustino Redondo (Servcio de Urgencias Canario (SUC), Las Palmas de Gran Canaria, Spain), Cesar Manuel Guerra García (061 Cantabria, Santander, Spain), Juan Valenciano Rodriguez (Gerencia de Urgencias, Emergencias y Transporte Sanitario, Toledo, Spain), Juan José Lara (Gerencia de Urgencias, Emergencias y Transporte Sanitario, Toledo, Spain), Cristina Martinez-Villalobos Aguilar (Gerencia de Urgencias, Emergencias y Transporte Sanitario, Toledo, Spain), Carmen del Pozo Pérez (Servicio de Emergencias Sanitarias de Castilla y Leon, Valladolid, Spain), Almudena Noriega Miguez (Servicio de Emergencias Sanitarias de Castilla y Leon, Valladolid, Spain), José Javier García Cortés (Servicio de Emergencias Sanitarias de Castilla y Leon, Valladolid, Spain), Francesc Xavier Jimenez Fabrega (Sistema d'Emergències Mèdiques de Catalunya, Barcelona, Spain; Institut d'Investigació Sanitaria Pere i Virgili (IISPV), Tarragona, Spain), Xabier Escalada Roig (Sistema d'Emergències Mèdiques de Catalunya, Barcelona, Spain), Youcef Azeli (Sistema d'Emergències Mèdiques de Catalunya, Barcelona, Spain; Institut d'Investigació Sanitaria Pere i Virgili (IISPV), Tarragona, Spain), Silvia Sola-Muñoz (Sistema d'Emergències Mèdiques de Catalunya, Barcelona, Spain; Institut d'Investigació Sanitaria Pere i Virgili (IISPV), Tarragona, Spain), María C. Escriche (SAMU Comunidad Valenciana, Valencia, Spain), Ana Forner Canós (SAMU Comunidad Valenciana, Valencia, Spain), Vanessa Tomàs (SAMU Comunidad Valenciana, Valencia, Spain), Carlos Sanchis (SAMU Comunidad Valenciana, Valencia, Spain), Jose Luis Nieto (SAMU Comunidad Valenciana, Valencia, Spain), Itziar Ilzarbe (SAMU Comunidad Valenciana, Valencia, Spain), Cristian Fernández Barreras (Emergencias Osakidetza, Euzkadi, Spain), Fernando Vicente Casanova (Emergencias Osakidetza, Euzkadi, Spain), Susana Batres Gomez (Emergencias Sanitarias extrahospitalarias de Extremadura, ESEX 112, Extremadura, Spain), Begoña Gomez Pérez (Emergencias Sanitarias extrahospitalarias de Extremadura, ESEX 112, Extremadura, Spain), Pedro Jesús Martín Hernández (Emergencias Sanitarias extrahospitalarias de Extremadura, ESEX 112, Extremadura, Spain), Jose Manuel Hernández Royano (Emergencias Sanitarias extrahospitalarias de Extremadura, ESEX 112, Extremadura, Spain), Francisco Javier Medina Aragón (Emergencias Sanitarias extrahospitalarias de Extremadura, ESEX 112, Extremadura, Spain), Jose Antonio Iglesias Vazquez (Fundacion Publica Urxencias Sanitarias de Galicia 061, Santiago de Compostela, Spain), Pedro Dacal Pérez (Fundacion Publica Urxencias Sanitarias de Galicia 061, Santiago de Compostela, Spain), Xesús María López Alvarez (Fundacion Publica Urxencias Sanitarias de Galicia 061, Santiago de Compostela, Spain), Marta Dorribo Masid (Fundacion Publica Urxencias Sanitarias de Galicia 061, Santiago de Compostela, Spain), Marcos Juanes (Servicio Emergencias Sanitarias de La Rioja, Logroño, Spain), María José García-Ochoa Blanco (SAMUR PC Madrid, Madrid, Spain), Natividad Ramos Garcia (SAMUR PC Madrid, Madrid, Spain), Carmen Camacho Leis (SAMUR PC Madrid, Madrid, Spain), Jose María Navalpotro Pascual (Servicio Urgencias Medicas Madrid, Madrid, Spain), Alicia Villar Arias (Servicio Urgencias Medicas Madrid, Madrid, Spain), Francisco Jose Peinado (Servicio Urgencias Medicas Madrid, Madrid, Spain), Francisco Angel Guirao Salinas (Servicio de Emergencias 061 Murcia, Murcia, Spain), Cruz Lopez Perez (Servicio de Emergencias 061 Murcia, Murcia, Spain), Alfredo Echarri Sucunza (Servicio de urgencias extrahospitalarias de Navarra, Pamplona, Spain), Junior Jose García Mendoza (Servicio de urgencias extrahospitalarias de Navarra, Pamplona, Spain), Jose Antonio Cortes Ramas (Servicio de Bomberos de Zaragoza, Zaragoza, Spain), Miguel Artigas (Servicio de Bomberos de Zaragoza, Zaragoza, Spain), Patricia Fernandez del Valle (Agencia de Servicios Sociales y Dependencia de Andalucía, Sevilla, Spain), Inamcualda Mateo (Escuela Andaluza de Salud Pública - CIBERESP, Granada, Spain), Félix Rivera Sánz (Fundacion Rioja Salud - Unidad de la Ciencia del dato, Logroño, Spain), Sara Bendotti (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Alessia Currao (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Francesca Romana Gentile (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Sara Compagnoni (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Federico Quilico (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Luca Vicini Scajola (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Clara Lopiano (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Alessandro Fasolino (Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Giuseppe Maria Sechi (Agenzia Regionale Emergenza Urgenza, Milano – AREU Lombardia, Italy), Gianluca Marconi (Agenzia Regionale Emergenza Urgenza, Milano – AREU Lombardia, Italy), Gianluca Panni (AAT Brescia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Degli Spedali Civili di Brescia, Brescia, Italy), Davide Sgotti (AAT Brescia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Degli Spedali Civili di Brescia, Brescia, Italy), Ettore Zorzi (AAT Como—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Lariana (CO), Como, Italy), Marco Cazzaniga (AAT Como—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Lariana (CO), Como, Italy), Umberto Piccolo

(AAT Como—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Lariana (CO), Como, Italy), Daniele Bussi (AAT Cremona—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Cremona, Cremona, Italy), Simone Ruggeri (AAT Cremona—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Cremona, Cremona, Italy), Fabio Facchin (AAT Mantova—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Mantova, Mantova, Italy), Edoardo Soffiato (AAT Mantova—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Mantova, Mantova, Italy), Vincenza Ronchi (AAT Pavia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Pavia, Pavia, Italy), Enrico Contri (AAT Pavia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Pavia, Pavia, Italy), Paola Centineo (AAT Varese—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST dei Sette Laghi, Varese, Italy), Francesca Reali (AAT Lodi—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Lodi, Lodi, Italy), Maurizio Migliori (Agenzia Regionale Emergenza Urgenza, Milano – AREU Lombardia, Italy), Guido Matiz (Agenzia Regionale Emergenza Urgenza, Milano – AREU Lombardia, Italy), Andrea Pagliosa (Agenzia Regionale Emergenza Urgenza, Milano – AREU Lombardia, Italy), Marco Botteri (AAT Brescia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Degli Spedali Civili di Brescia, Brescia, Italy), Matteo Caresani (Sala Operativa Regionale Emergenza Urgenza dei Laghi – AREU Lombardia, Como, Italy), Dario Franchi (Sala Operativa Regionale Emergenza Urgenza dei Laghi – AREU Lombardia, Como, Italy), Marco Paiella (AAT Como—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Lariana (CO), Como, Italy), Giovanni Vaghini (AAT Como—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Lariana (CO), Como, Italy), Sabina Campi (AAT Varese—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST dei Sette Laghi, Varese, Italy), Fabrizio Canevari (Sala Operativa Regionale Emergenza Urgenza della Pianura – AREU Lombardia, Pavia, Italy), Antonella Brancaglione (Sala Operativa Regionale Emergenza Urgenza della Pianura – AREU Lombardia, Pavia, Italy), Alessandra Palo (AAT Pavia—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST Pavia, Pavia, Italy), Giuseppe Bergamini (AAT Lodi—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Lodi, Lodi, Italy), Ugo Rizzi (AAT Cremona—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Cremona, Cremona, Italy), Pierpaolo Parogni (AAT Mantova—Agenzia Regionale Emergenza Urgenza (AREU) c/o ASST di Mantova, Mantova, Italy), Diego Maffeo (Fondazione Poliambulanza di Brescia, Brescia, Italy), Alessio Stanzione (Fondazione Poliambulanza di Brescia, Brescia, Italy), Daniele Ghiraldin (Spedali Civili di Brescia, Brescia, Italy), Marta Ruffinazzi (Ospedale Sant'Anna di Como, Como, Italy), Cecilia Fantoni (Ospedale "Mater Domini" di Castellanza, Castellanza, Italy), Cinzia Dossena (Ospedale Maggiore di Crema, Crema, Italy), Luigi Moschini (Ospedale di Cremona, Cremona, Italy), Silvia Affinito (Ospedale di Legnano, Legnano, Italy), Claudio Vimercati (Ospedale di Legnano, Legnano, Italy), Irene Raimondi Cominesi (Ospedale Maggiore di Lodi, Lodi, Italy), Cristian Fava (Ospedale "Carlo Poma" di Mantova, Mantova, Italy), Roberta Bertona (Ospedale Civile di Vigevano, Vigevano, Italy), Fabrizio Giofré (Ospedale Civile di Voghera, Voghera, Italy), Roberto De Ponti (Ospedale di Circolo e Fondazione Macchi di Varese, ASST dei Sette Laghi, Varese, Italy), Ivan Caico (ASST Valle Olona), Alessandra Russo (ASST Valle Olona), Valeria Musella (Biostatistics & Clinical Trial Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Moreno Curti (Biostatistics & Clinical Trial Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy), Andrea Lorenzo Vecchi (ASST dei Sette Laghi, Varese, Italy), Battistina Castiglioni (ASST dei Sette Laghi, Varese, Italy), Paola Genoni (ASST dei Sette Laghi, Varese, Italy), Carlo Arnò (ASST dei Sette Laghi, Varese, Italy), Andrea Piemonti (ASST dei Sette Laghi, Varese, Italy), Cinzia Franzosi (ASST dei Sette Laghi, Varese, Italy), Fulvio Giovenzana (ASST dei Sette Laghi, Varese, Italy)

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2023.110043.

Author details

the OHCA-COVID study group [a]Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy [b]Cardiac Arrest and Resuscitation Science Research Team (RESTART), Fondazione IRCCS Policlinico San Matteo, Pavia, Italy [c]Biostatistics & Clinical Trial Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy [d]Department of Medicine, Saint Luke's Mid America Heart Institute, Kansas City, USA [e]Departments of Emergency Medicine, Critical Care Medicine and Neurology, University of Pittsburgh, Pittsburgh, USA [f]Centre of Cardiovascular Research & Education in Therapeutics (CCRET), School of Public Health and Preventive Medicine, Monash University, Clayton, Australia [g]Baker Heart and Diabetes Institute, Melbourne, Australia [h]Centre for Research and Evaluation, Ambulance Victoria, Melbourne, Australia [i]University of Washington School of Medicine, Seattle, USA [j]Seattle Fire Department, Seattle, USA [k]Servicio de Emergencias 061 de La Rioja, Centro de Investigación Biomédica de La Rioja (CIBIR), Logroño, Spain [l]Clinical Audit & Research Unit, London Ambulance Service NHS Trust, London, UK [m]Fondazione Ticino Cuore, Lugano, Switzerland [n]Faculty of Biomedical Sciences, Università della Svizzera Italiana (USI), Lugano, Switzerland [o]Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale, Lugano, Switzerland [p]Centrale Operativa Provinciale SUEM 118, Azienda ULSS 5 Polesana, Rovigo, Italy[q]Division of Cardiology, European Georges Pompidou Hospital, Paris, France[r]Emory University School of Medicine, Rollins School of Public Health, Atlanta, USA[s]Public Health – Seattle & King County, Seattle, USA [t]Federazione Cantonale Ticinese Servizi Autoambulanze, Lugano, Switzerland[u]Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy [v]Emory University, Woodruff Health Sciences Center, Atlanta, USA [w]Andalusian School of Public Health, CIBER Epidemiology and Public Health (CIBERESP), Granada, Spain

REFERENCES

[1]. Nishiyama C, Kiguchi T, Okubo M, et al. Three-year trends in out-of-hospital cardiac arrest across the world: Second report from the International Liaison Committee on Resuscitation (ILCOR). Resuscitation. December 2022;2023. https://doi.org/10.1016/j.resuscitation.2023.109757 109757.

[2]. Kiguchi T, Okubo M, Nishiyama C, et al. Out-of-hospital cardiac arrest across the World: First report from the International Liaison Committee on Resuscitation (ILCOR). Resuscitation.

2020;152:39–49. https://doi.org/10.1016/j.resuscitation.2020.02.044.
[3]. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727–33. https://doi.org/10.1056/NEJMoa2001017.
[4]. Fauci AS, Lane HC, Redfield RR. Covid-19 - Navigating the uncharted. N Engl J Med. 2020;382:1268–9. https://doi.org/10.1056/NEJMe2002387.
[5]. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed. 2020;91:157–60. https://doi.org/10.23750/abm.v91i1.9397.
[6]. Baldi E, Sechi GM, Mare C, et al. Out-of-hospital cardiac arrest during the COVID-19 outbreak in Italy. N Engl J Med. 2020;383:496–8. https://doi.org/10.1056/NEJMc2010418.
[7]. Baldi E, Sechi GM, Mare C, et al. COVID-19 kills at home: The close relationship between the epidemic and the increase of out-of-hospital cardiac arrests. Eur Heart J. 2020;41:3045–54. https://doi.org/10.1093/eurheartj/ehaa508.
[8]. Baldi E, Sechi GM, Mare C, et al. Treatment of out-of-hospital cardiac arrest in the COVID-19 era: A 100 days experience from the Lombardy region. PLoS One. 2020;15. https://doi.org/10.1371/journal.pone.0241028.
[9]. Marijon E, Karam N, Jost D, et al. Out-of-hospital cardiac arrest during the COVID-19 pandemic in Paris, France: a population-based, observational study. Lancet Public Heal. 2020;5:e437–43. https://doi.org/10.1016/S2468-2667(20)30117-1.
[10]. Uy-Evanado A, Chugh HS, Sargsyan A, et al. Out-of-Hospital Cardiac Arrest Response and Outcomes During the COVID-19 Pandemic. JACC Clin Electrophysiol. 2021;7:6–11. https://doi.org/10.1016/j.jacep.2020.08.010.
[11]. Prezant DJ, Lai PH, Lancet EA, et al. Characteristics Associated with Out-of-Hospital Cardiac Arrests and Resuscitations during the Novel Coronavirus Disease 2019 Pandemic in New York City. JAMA Cardiol. 2020;5:1154–63. https://doi.org/10.1001/jamacardio.2020.2488.
[12]. Holland M, Burke J, Hulac S, et al. Excess Cardiac Arrest in the Community During the COVID-19 Pandemic. JACC Cardiovasc Interv. 2020;13:1968–9. https://doi.org/10.1016/j.jcin.2020.06.022.
[13]. Nickles AV, Oostema A, Allen J, O'Brien SL, Demel SL, Reeves MJ. Comparison of Out-of-Hospital Cardiac Arrests and Fatalities in the Metro Detroit Area during the COVID-19 Pandemic with Previous-Year Events. JAMA Netw Open. 2021;4:2020–3. https://doi.org/10.1001/jamanetworkopen.2020.32331.
[14]. Cho JW, Jung H, Lee MJ, et al. Preparedness of personal protective equipment and implementation of new CPR strategies for patients with out-of-hospital cardiac arrest in the COVID-19 era. Resusc Plus. 2020;3. https://doi.org/10.1016/j.resplu.2020.100015 100015.
[15]. Ball J, Nehme Z, Bernard S, Stub D, Stephenson M, Smith K. Collateral damage: Hidden impact of the COVID-19 pandemic on the out-of-hospital cardiac arrest system-of-care. Resuscitation. 2020;156:157–63. https://doi.org/10.1016/j.resuscitation.2020.09.017.
[16]. Elmer J, Okubo M, Guyette FX, Martin-Gill C. Indirect effects of COVID-19 on OHCA in a low prevalence region. Resuscitation. 2020;156:282–3. https://doi.org/10.1016/j.resuscitation.2020.08.127.
[17]. Rosell Ortiz F, Fernández del Valle P, Knox EC, et al. Influence of the Covid-19 pandemic on out-of-hospital cardiac arrest. A Spanish nationwide prospective cohort study. Resuscitation. 2020;157:230–40. https://doi.org/10.1016/j.resuscitation.2020.09.037.
[18]. Sayre MR, Barnard LM, Counts CR, et al. Prevalence of COVID-19 in Out-of-Hospital Cardiac Arrest: Implications for Bystander Cardiopulmonary Resuscitation. Circulation. 2020;142:507–9. https://doi.org/10.1161/CIRCULATIONAHA.120.048951.
[19]. Semeraro F, Gamberini L, Tartaglione M, et al. Out-of-hospital cardiac arrest during the COVID-19 era in Bologna: System response to preserve performances. Resuscitation. 2020;157:1–2. https://doi.org/10.1016/j.resuscitation.2020.09.032.
[20]. Paoli A, Brischigliaro L, Scquizzato T, Favaretto A, Spagna A. Out-of-hospital cardiac arrest during the COVID-19 pandemic in the Province of Padua, Northeast Italy. Resuscitation 2020;154:47–9. https://doi.org/10.1016/j.resuscitation.2020.06.031.
[21]. Chan PS, Girotra S, Tang Y, Al-Araji R, Nallamothu BK, McNally B. Outcomes for Out-of-Hospital Cardiac Arrest in the United States during the Coronavirus Disease 2019 Pandemic. JAMA Cardiol. 2021;6:296–303. https://doi.org/10.1001/jamacardio.2020.6210.
[22]. Ng QX, Lee EZH, Tay JAM, Arulanandam S. Impact of COVID-19 'circuit-breaker' measures on emergency medical services utilisation and out-of-hospital cardiac arrest outcomes in Singapore. EMA - Emerg Med Australas. 2021;33:149–51. https://doi.org/10.1111/1742-6723.13668.
[23]. Baldi E, Auricchio A, Klersy C, et al. Out-of-hospital cardiac arrests and mortality in Swiss Cantons with high and low COVID-19 incidence: A nationwide analysis. Resusc Plus. 2021;6. https://doi.org/10.1016/j.resplu.2021.100105 100105.
[24]. Baldi E, Primi R, Bendotti S, et al. Relationship between out-of-hospital cardiac arrests and COVID-19 during the first and second pandemic wave. The importance of monitoring COVID-19 incidence. PLoS One. 2021;16. https://doi.org/10.1371/journal.pone.0260275.
[25]. Chugh HS, Sargsyan A, Nakamura K, et al. Sudden Cardiac Arrest During the COVID-19 Pandemic: A Two-Year Prospective Evaluation in a North American Community. Hear Rhythm. Published online 2023. https://doi.org/10.1016/j.hrthm.2023.03.025.
[26]. Cummins R 0., Ornato JP, Thies WH, Pepe PE. Improving Survival From Sudden Cardiac Arrest: The "Chain of Survival" Concept. Circ AHA Statement. 1991;83:1831-1843. http://circ.ahajournals.org/content/122/18_suppl_3/S787.
[27]. Baert V, Jaeger D, Hubert H, et al. Assessment of changes in cardiopulmonary resuscitation practices and outcomes on 1005 victims of out-of-hospital cardiac arrest during the COVID-19 outbreak: registry-based study. Scand J Trauma Resusc Emerg Med. 2020;28:1–10. https://doi.org/10.1186/s13049-020-00813-x.
[28]. Fothergill RT, Smith AL, Wrigley F, Perkins GD. Out-of-Hospital Cardiac Arrest in London during the COVID-19 pandemic. Resusc Plus. 2021;5. https://doi.org/10.1016/j.resplu.2020.100066 100066.
[29]. Cho JW, Jung H, Lee MJ, et al. Preparedness of personal protective equipment and implementation of new CPR strategies for patients with out-of-hospital cardiac arrest in the COVID-19 era. Resusc Plus. 2020;3. https://doi.org/10.1016/j.resplu.2020.100015.
[30]. Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: Rationale, conduct, and reporting. BMJ. 2010;340:521–5. https://doi.org/10.1136/bmj.c221.
[31]. Stewart LA, Clarke M, Rovers M, et al. Preferred reporting items for a systematic review and meta-analysis of individual participant data: The PRISMA-IPD statement. JAMA - J Am Med Assoc. 2015;313:1657–65. https://doi.org/10.1001/jama.2015.3656.
[32]. Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: Update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest: A statement for healthcare professionals from a task force of the international liaison committee. Circulation. 2015;132:1286–300. https://doi.org/10.1161/CIR.0000000000000144.
[33]. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. (Available from URL https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). Published online 2012. doi:10.2307/632432.
[34]. Charlton K, Limmer M, Moore H. Incidence of emergency calls and out-of-hospital cardiac arrest deaths during the COVID-19 pandemic: Findings from a cross-sectional study in a UK ambulance service. Emerg Med J. 2021;38:446–9. https://doi.org/10.1136/emermed-2020-210291.

[35]. Greene A, Sapp J, Hirsch G, et al. Cardiovascular Outcomes in Nova Scotia during the Early Phase of the COVID-19 Pandemic. CJC Open. Published online 2021. https://doi.org/10.1016/j.cjco.2021.12.008.
[36]. Guimarães NS, Carvalho TML, Machado-Pinto J, et al. Increased home death due to cardiopulmonary arrest in times of covid-19 pandemic. Arq Bras Cardiol. 2021;116:266–71. https://doi.org/10.36660/abc.20200547.
[37]. Ahn JY, Ryoo HW, Cho JW, Kim JH, Lee SH, Jang TC. Impact of the covid-19 outbreak on adult out-of-hospital cardiac arrest outcomes in daegu, south korea: An observational study. Clin Exp Emerg Med. 2021;8:137–44. https://doi.org/10.15441/ceem.21.008.
[38]. Yu JH, Liu CY, Chen WK, et al. Impact of the COVID-19 pandemic on emergency medical service response to out-of-hospital cardiac arrests in Taiwan: A retrospective observational study. Emerg Med J. 2021;38:679–84. https://doi.org/10.1136/emermed-2020-210409.
[39]. Ball J, Nehme Z, Bernard S, Stub D, Stephenson M, Smith K. Collateral damage: Hidden impact of the COVID-19 pandemic on the out-of-hospital cardiac arrest system-of-care. Resuscitation. 2020;156:157–63. https://doi.org/10.1016/j.resuscitation.2020.09.017.
[40]. Shadbolt N, Brett A, Chen M, et al. The challenges of data in future pandemics. Epidemics. 2022:40. https://doi.org/10.1016/j.epidem.2022.100612.
[41]. Lüscher TF. Understanding COVID-19: In the end it is the endothelium-what else? Eur Heart J. 2020;41:3023–7. https://doi.org/10.1093/eurheartj/ehaa706.
[42]. Price S, Singh S, Ledot S, et al. Respiratory management in severe acute respiratory syndrome coronavirus 2 infection. Eur Hear journal Acute Cardiovasc care. Published online 2020. https://doi.org/10.1177/2048872620924613.
[43]. Tan HL. How does COVID-19 kill at home and what should we do about it? Eur Heart J. 2020;41:3055–7. https://doi.org/10.1093/eurheartj/ehaa599.
[44]. Baldi E, Savastano S. Fear of contagion: One of the most devious enemies to fight during the COVID-19 pandemic. Disaster Med Public Health Prep. 2021;15:E8–9. https://doi.org/10.1017/dmp.2020.338.
[45]. Al Amiry A, Maguire BJ. Emergency medical services (Ems) calls during covid-19: Early lessons learned for systems planning (a narrative review). Open Access Emerg Med. 2021;13:407–14. https://doi.org/10.2147/OAEM.S324568.
[46]. Parmet WE, Sinha MS. Covid-19 - The law and limits of quarantine. N Engl J Med. 2020;382:E281–3. https://doi.org/10.1056/NEJMp2004211.
[47]. Baldi E, Cortegiani A, Savastano S. Cardiac arrest and coronavirus disease 2019. Curr Opin Crit Care. 2022;28:237–43. https://doi.org/10.1097/MCC.0000000000000931.
[48]. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506. https://doi.org/10.1016/S0140-6736(20)30183-5.
[49]. Waalewijn RA, Nijpels MA, Tijssen JG, Koster RW. Prevention of deterioration of ventricular fibrillation by basic life support during out-of-hospital cardiac arrest. Resuscitation. 2002;54:31–6. https://doi.org/10.1016/S0300-9572(02)00047-3.
[50]. Savastano S, Vanni V. Cardiopulmonary resuscitation in real life: The most frequent fears of lay rescuers. Resuscitation. 2011;82:568–71. https://doi.org/10.1016/j.resuscitation.2010.12.010.
[51]. Baldi E, Bertaia D, Savastano S. Mouth-to-mouth: An obstacle to cardio-pulmonary resuscitation for lay-rescuers. Resuscitation. 2014;85:e195–6. https://doi.org/10.1016/j.resuscitation.2014.10.001.
[52]. Hawkes CA, Brown TP, Booth S, et al. Attitudes to cardiopulmonary resuscitation and defibrillator use: A survey of UK adults in 2017. J Am Heart Assoc. 2019;8. https://doi.org/10.1161/JAHA.117.008267.
[53]. B M Tjelmeland I, Wnent J, Masterson S, et al. Did lockdown influence bystanders' willingness to perform cardiopulmonary resuscitation? A worldwide registry-based perspective. Resuscitation. 2023;(February):109764. https://doi.org/10.1016/j.resuscitation.2023.109764.
[54]. Baldi E, Caputo ML, Savastano S, et al. An Utstein-based model score to predict survival to hospital admission: The UB-ROSC score. Int J Cardiol. 2020;308:84–9. https://doi.org/10.1016/j.ijcard.2020.01.032.
[55]. Park JH, Song KJ, Do Shin S, Hong KJ. The impact of COVID-19 pandemic on out-of-hospital cardiac arrest system-of-care: Which survival chain factor contributed the most? Am J Emerg Med. 2023;63:61–8. https://doi.org/10.1016/j.ajem.2022.10.023.
[56]. Guerini Giusteri V, Caputo ML, Baldi E, Auricchio A, Savastano S. Effect of COVID-19 on out-of-hospital cardiac arrest survival: no light at the end of the tunnel yet. Resuscitation. Published online 2023:in press.