Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

RESUSCITATION 173 (2022) 71–75

Available online at ScienceDirect

Resuscitation

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

Short paper

Outcomes of pediatric patients with COVID-19 and in-hospital cardiopulmonary resuscitation

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Abstract

Background: Early studies found low survival rates for adults with COVID-19 infection and in-hospital cardiac arrest (IHCA). We evaluated the association of COVID-19 infection on survival outcomes in pediatric patients undergoing cardiopulmonary resuscitation (CPR).

Methods: Within Get-With-The-Guidelines®-Resuscitation, we identified pediatric patients who underwent CPR for an IHCA or bradycardia with poor perfusion between March and December, 2020. We compared survival outcomes (survival to discharge and return of spontaneous circulation for ≥20 minutes [ROSC]) between patients with suspected/confirmed COVID-19 infection and non-COVID-19 patients using multivariable hierarchical regression, with hospital site as a random effect and patient and cardiac arrest variables with a significant ($p < 0.05$) bivariate association as fixed effects.

Results: Overall, 1328 pediatric in-hospital CPR events were identified (590 IHCA, 738 bradycardia with poor perfusion), of which 46 (32 IHCA, 14 bradycardia) had suspected/confirmed COVID-19 infection. Rates of survival to discharge were similar between those with and without COVID-19 infection (39.1% vs. 44.9%; adjusted RR, 1.14 [95% CI: 0.55–2.36]), and these estimates were similar for those with IHCA and bradycardia with poor perfusion (adjusted RRs of 1.03 and 1.05; interaction $p = 0.96$). Rates of ROSC were also similar between pediatric patients with and without COVID-19 overall (67.4% vs. 76.9%; adjusted RR, 0.87 [0.43, 1.77]), and for the subgroups with IHCA or bradycardia requiring CPR (adjusted RRs of 0.95 and 0.86, interaction $p = 0.26$).

Conclusions: In a large multicenter national registry of CPR events, COVID-19 infection was not associated with lower rates of ROSC or survival to hospital discharge in pediatric patients undergoing CPR.

Keywords: In-hospital cardiac arrest, COVID-19, Cardiopulmonary resuscitation, Pediatric cardiac arrest

Introduction

Although coronavirus disease 2019 (COVID-19) has been described primarily as a mild disease in children, rates of pediatric hospitalizations of patients with COVID-19 are on the rise.[1] The hospital course of pediatric patients may be complicated by clinical decompensation and potentially progress to in-hospital cardiac arrest (IHCA), yet little information is currently available on outcomes of pediatric patients with COVID-19 undergoing cardiopulmonary resuscitation (CPR).

Abbreviations: IHCA, in-hospital cardiac arrest, COVID-19, coronavirus disease 2019, CPR, cardiopulmonary resuscitation, GWTG-R, Get With The Guidelines Resuscitation Registry

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https://doi.org/10.1016/j.resuscitation.2022.02.018
Received 24 November 2021; Received in Revised form 15 February 2022; Accepted 20 February 2022

In adults with COVID-19 infection, previous reports have described low survival rates for those with IHCA.[2–4] Besides the physiologic effects of COVID-19 infection, other potential reasons for lower survival in adults with IHCA include delays in CPR initiation due to requirements of donning personal protective equipment, shorter duration of resuscitation efforts, and overall decrease in CPR quality.[5,6] Although it would be reasonable to believe that pediatric patients with COVID-19 who undergo CPR would have lower survival than children without COVID-19, there is a need for empirical data to quantify the extent of lower survival with COVID-19 infection in this population. Accordingly, within a large national registry, we examined the association of COVID-19 infection on survival outcomes for pediatric patients who underwent CPR.

Methods

The study was approved by Saint Luke's Hospital's IRB, which waived the requirement for informed consent as the study involved deidentified data.

Study design

Get With The Guidelines® (GWTG)-Resuscitation is a large, prospective, quality improvement registry of IHCA and CPR events. The registry design has been previously described.[7] In brief, trained hospital personnel identify all patients without do-not-resuscitate orders who undergo cardiopulmonary resuscitation. Cases are identified by centralized collection of cardiac arrest flow sheets, reviews of hospital paging system logs, and routine checks of code carts and pharmacy tracer drug records.[7] Standardized Utstein-style definitions are used for all patient variables and outcomes to facilitate uniform reporting across hospitals.[8,9]

Within GWTG-Resuscitation, we identified patients under 18 years of age between March 1 and December 31, 2020, with an in-hospital CPR event due to a pulseless IHCA or bradycardia with poor perfusion requiring CPR. The independent variable was whether the pediatric patient had suspected/confirmed COVID-19 infection at the time of their CPR event. Our primary outcome was survival to discharge, and the secondary outcome was sustained return of spontaneous circulation for $\geq$20 minutes (ROSC).

Statistical analysis

Baseline characteristics of patients with and without COVID-19 were compared using Fisher's exact test for categorical variables and student's *t*-test for continuous variables.

In the overall cohort, we compared rates of survival to discharge between patients with and without COVID-19 infection by constructing multivariable hierarchical regression models, with hospital site as a random effect and COVID-19 status, location of arrest, and initial rhythm, regardless of statistical significance as fixed effects. Because of the sample size, we only included the following other variables with a bivariate association as fixed effects to avoid overparameterization: age, sex, race, initial cardiac arrest rhythm, location of cardiac arrest, comorbid conditions (prior heart failure or myocardial infarction, index admission heart failure or myocardial infarction, diabetes mellitus, baseline depression in central nervous system function, acute stroke, pneumonia, and metastatic or hematologic malignancy), medical conditions present within 24 hours of cardiac arrest (renal insufficiency, hepatic insufficiency, respiratory insufficiency, hypotension, septicemia, and metabolic or electrolyte abnormality), and interventions in place at the time of cardiac arrest (continuous intravenous vasopressor, assisted or mechanical ventilation, and hemodialysis). These models used a Poisson distribution with a log-link to estimate risk ratios (RRs). We then evaluated for an interaction between COVID-19 status and CPR event type (IHCA vs. bradycardia with poor perfusion) to determine if the association between COVID-19 and survival differed for IHCA and bradycardia events. Finally, we repeated all analyses for the secondary outcome of ROSC.

For each analysis, the null hypothesis was evaluated at a 2-sided significance level of 0.05 and calculated 95% confidence intervals (CIs) using robust standard errors. All statistical analyses were conducted using SAS Version 9.1.3 (SAS Institute, Cary, NC).

Results

Of 1328 pediatric in-hospital CPR events, 590 were pulseless IHCAs and 738 were bradycardia requiring CPR. Suspected/confirmed COVID-19 infection was present in 46 patients (17 confirmed, 6 suspected, and 23 were missing designation as confirmed or suspected). Of these 46 with suspected/confirmed COVID-19 infection, 32 (5.4%) had IHCA and 14 (1.9%) had bradycardia requiring CPR. Patient and cardiac arrest characteristics by COVID-19 status and CPR event type (pulseless IHCA and bradycardia with poor perfusion) are summarized in Table 1. Both cohorts were similar in age groups, sex, race/ethnicity, and an initial non-shockable cardiac arrest rhythm. Compared with non-COVID-19 patients, COVID-19 patients were more likely to have sepsis, pneumonia, and renal insufficiency. Rates of continuous intravenous vasopressor agents, invasive mechanical ventilation, and hemodialysis at the time of arrest were comparable in both groups.

Overall, 18 (39.1%) COVID-19 patients with a CPR event survived to discharge as compared with 576 (44.9%) non-COVID-19 patients. After multivariable adjustment, COVID-19 infection was not associated with survival to discharge overall (adjusted RR, 1.14 [95% CI: 0.55, 2.36), and this was the case separately for patients with IHCA and bradycardia requiring CPR (adjusted RRs of 1.03 and 1.05, respectively; interaction p-value: 0.96; Table 2). COVID-19 infection was also not associated with reduced rates of ROSC as compared to non-COVID-19 patients (67.4% vs. 76.9%; adjusted RR, 0.87 [0.43, 1.77]), with no difference in ROSC rates for patients with either IHCA or bradycardia requiring CPR (adjusted RRs of 0.95 and 0.86, respectively; interaction *p*-value: 0.26).

Discussion

Among pediatric patients requiring CPR during the pandemic months in 2020, COVID-19 infection was not associated with lower rates of ROSC or survival to discharge. This was the case overall, and for those with IHCA or bradycardia with poor perfusion. Our results on the association between COVID-19 infection and survival differ from those for IHCA in adult patients, which ranged from 0% to 14%.[10,11]

One reason for the difference in results is potentially less severe illness with COVID-19 in hospitalized pediatric patients undergoing CPR as compared to adults. In our study, there were no differences in rates of mechanical ventilation between pediatric patients requiring CPR with and without COVID-19 infection although there were higher rates of pneumonia and sepsis in pediatric patients with

Table 1 – Baseline characteristics of patients with and without COVID-19 infection.*

		Pulseless IHCA (*N* = 590)			Bradycardia (*N* = 738)		
	Total *N* = 1328	No COVID-19 (*n* = 558)	COVID-19 + (*n* = 32)	*P*	No COVID-19 (*n* = 724)	COVID-19 + (*n* = 14)	*P*
DEMOGRAPHICS							
Age group							
Newly born	359 (27.0)	61 (10.9)	3 (9.4)	0.66	293 (40.5)	2 (14.3)	0.02
Neonates	430 (32.4)	153 (27.4)	7 (21.9)		266 (36.7)	4 (28.6)	
>1 month to 8 years	285 (21.5)	160 (28.7)	8 (25.0)		112 (15.5)	5 (35.7)	
>8 to <18 years	254 (19.1)	184 (33.0)	14 (43.8)		53 (7.3)	3 (21.4)	
Female sex	592 (44.6)	260 (46.6)	17 (53.1)	0.59	309 (42.7)	6 (42.9)	1.00
Race							
White	599 (45.1)	255 (45.7)	10 (31.3)	0.06	331 (45.7)	3 (21.4)	0.17
Black	337 (25.4)	132 (23.7)	13 (40.6)		187 (25.8)	5 (35.7)	
Other	70 (5.3)	37 (6.6)	0 (0.0)		33 (4.6)	0 (0.0)	
Unknown	322 (24.3)	134 (24.0)	9 (28.1)		173 (23.9)	6 (42.9)	
Hispanic ethnicity	216 (16.3)	99 (17.7)	5 (15.6)	0.76	110 (15.2)	2 (14.3)	1.00
CARDIAC ARREST FACTORS							
Location of arrest							
Intensive care unit	1028 (77.4)	379 (67.9)	27 (84.4)	0.13	612 (84.5)	10 (71.4)	0.19
Telemetry unit	7 (0.5)	6 (1.1)	0 (0.0)		1 (0.1)	0 (0.0)	
Non-monitored hospital unit	54 (4.1)	33 (5.9)	0 (0.0)		19 (2.6)	2 (14.3)	
Emergency room	116 (8.7)	84 (15.1)	4 (12.5)		27 (3.7)	27 (3.7)	
Procedural area	111 (8.4)	52 (9.3)	0 (0.0)		58 (8.0)	58 (8.0)	
Other	12 (0.9)	4 (0.7)	1 (3.1)		7 (1.0)	7 (1.0)	
Time of Arrest							
Night (11 PM to 6:59 AM)	371 (28.1)	159 (28.6)	8 (25.0)	0.84	201 (28.0)	3 (21.4)	0.77
Weekend	378 (28.5)	167 (29.9)	11 (34.4)	0.56	197 (27.2)	3 (21.4)	0.77
Initial Cardiac Arrest Rhythm							
Asystole	193 (14.5)	186 (33.3)	7 (21.9)	0.18	0 (0.0)	0 (0.0)	1.00
Pulseless electrical activity	338 (25.5)	314 (56.3)	24 (75)		0 (0.0)	0 (0.0)	
Ventricular fibrillation	21 (1.6)	21 (3.8)	0 (0.0)		0 (0.0)	0 (0.0)	
Pulseless ventricular tachycardia	38 (2.9)	37 (6.6)	1 (3.1)		0 (0.0)	0 (0.0)	
Bradycardia	738 (55.6)	0 (0.0)	0 (0.0)		724 (100)	14 (100)	
PRE-EXISTING CONDITIONS							
Cyanotic congenital heart disease	228 (17.2)	88 (15.8)	2 (6.3)	0.21	138 (19.1)	0 (0.0)	0.08
Heart failure this admission	48 (3.6)	20 (3.6)	1 (3.1)	0.89	27 (3.7)	0 (0.0)	1.00
Heart failure prior to admission	41 (3.1)	17 (3.1)	3 (9.4)	0.09	21 (2.9)	0 (0.0)	1.00
Myocardial infarction this admission	4 (0.3)	3 (0.5)	0 (0.0)	1.00	1 (0.1)	0 (0.0)	1.00
Myocardial infarction prior to admission	3 (0.2)	1 (0.2)	1 (3.1)	0.11	1 (0.1)	0 (0.0)	1.00
Hypotension	399 (30.1)	175 (31.4)	15 (46.9)	0.08	202 (27.9)	7 (50.0)	0.08
Respiratory insufficiency	947 (71.3)	366 (65.6)	21 (65.6)	1.00	547 (75.6)	13 (92.9)	0.21
Renal insufficiency	143 (10.8)	68 (12.2)	10 (31.3)	0.005	64 (8.8)	1 (7.1)	1.00
Hepatic insufficiency	50 (3.8)	31 (5.6)	4 (12.5)	0.11	15 (2.1)	0 (0.0)	1.00
Metabolic or electrolyte abnormality	332 (25.0)	146 (26.2)	12 (37.5)	0.22	171 (23.6)	3 (21.4)	1.00
Diabetes mellitus	24 (1.8)	17 (3.1)	5 (15.6)	0.005	2 (0.3)	0 (0.0)	1.00
Baseline depression in CNS function	212 (16.0)	101 (18.1)	5 (15.6)	0.72	102 (14.1)	4 (28.6)	0.13
Acute stroke	18 (1.4)	9 (1.6)	0 (0.0)	1.00	9 (1.2)	0 (0.0)	1.00
Acute CNS non-stroke event	146 (11.0)	77 (13.8)	6 (18.8)	0.43	63 (8.7)	0 (0.0)	0.62
Pneumonia	62 (4.7)	24 (4.3)	8 (25.0)	<0.001	28 (3.9)	2 (14.3)	0.11
Sepsis	189 (14.2)	65 (11.7)	12 (37.5)	<0.001	107 (14.8)	5 (35.7)	0.047
Metastatic or hematologic malignancy	46 (3.5)	33 (5.9)	2 (5.3)	1.00	11 (1.5)	0 (0.0)	1.00
INTERVENTIONS IN PLACE AT TIME OF ARREST							
Continuous intravenous vasopressor	537 (40.5)	316 (56.7)	16 (50.0)	0.47	448 (62.0)	9 (64.3)	1.00
Assisted or Mechanical ventilation	919 (69.3)	378 (68.0)	18 (56.3)	0.18	513 (70.9)	10 (71.4)	1.00
Hemodialysis	40 (3.0)	22 (3.9)	2 (6.3)	0.38	15 (2.1)	1 (7.1)	0.27

Abbreviation: CNS, central nervous system.

* Comparisons made with chi-square statistics or Fisher's exact test.

COVID-19. Less severe respiratory compromise in pediatric COVID-19 patients with a CPR event may account for the different associations of COVID-19 infection in pediatric and adult patients with CPR events. Although some have questioned whether CPR should even be initiated in adults with COVID-19 infection and IHCA,[12,13] our findings suggest that end-of-life decisions for pedi-

Table 2 – Association between COVID-19 infection and survival outcomes.

	COVID +	COVID −	Adjusted RR (95% CI)	*P*	Interaction *P*
SURVIVAL TO DISCHARGE					
Overall*	18/46 (39.1)	576/1282 (44.9)	1.14 (0.55, 2.36)	0.73	0.96
Pulseless IHCA†	10/32 (31.3)	208/558 (37.3)	1.03 (0.53, 2.00)	0.93	
Bradycardia‡	8/14 (57.1)	368/ 724 (50.8)	1.05 (0.52, 2.14)	0.89	
ROSC					
Overall*	31/46 (67.4)	986/1282 (76.9)	0.87 (0.43, 1.77)	0.71	0.26
Pulseless IHCA†	21/32 (65.6)	389/558 (69.7)	0.95 (0.60, 1.50)	0.83	
Bradycardia‡	10/14 (71.4)	597/724 (82.5)	0.86 (0.46, 1.62)	0.64	

Abbreviations: CI, confidence interval; IHCA, in-hospital cardiac arrest; RR, risk ratio; ROSC, return of spontaneous circulation for ≥20 minutes.

* Models for the overall cohort adjusted for COVID-19 status, initial rhythm, location of arrest, age group, pneumonia, sepsis, hypotension, and renal insufficiency.

† Models for IHCA adjusted for: COVID-19 status, initial rhythm, location of arrest, pneumonia, sepsis, and hypotension.

‡ Model for bradycardia adjusted for: COVID-19 status, location of arrest, hypotension, and sepsis.

atric patients with a CPR event should not be influenced by COVID-19 status.

To the best of our knowledge, one other report has described clinical outcomes of pediatric IHCA and COVID-19. Utilizing the PediRES-Q database, Lauridsen et al. evaluated 28 pediatric patients with confirmed or suspected COVID-19 who suffered IHCA between March 1, 2020 and April 1, 2021.[14] In their COVID-19 cohort, rates of ROSC and survival to discharge were 50% and 25%, respectively, which are comparatively lower than the rates in our cohort (67% and 39%). In contrast to our study, patients with COVID-19 in that study was associated with lower rates of ROSC although rates of survival to discharge were not significantly different. Our study extends the findings of this prior study by confirming that rates of survival to discharge were similar between children with and without COVID-19 infection who undergo a CPR event and by also examining the association of COVID-19 infection with survival outcomes after CPR for children with bradycardia with poor perfusion. Reasons for different results for ROSC between that and our study are unclear, but likely are due to different study populations and possibly variables in model adjustment.

Our study has the following limitations. As GWTG-Resuscitation is a quality improvement registry, our findings may not be representative of all hospitals. It is possible that some patients who were suspected to have COVID-19 were later confirmed to be negative. However, among 46 patients in our study with suspected/confirmed COVID-19 infection, we found that 74% of those with data on confirmed vs. suspected COVID-19 infection had confirmed COVID-19 infection, although there was a missing data rate of 50% on this optional data field. However, we found COVID-19 patients had higher rates of hypotension, pneumonia, and sepsis, which is consistent with active infection. Second, our sample of COVID-19 patients was small and may have been underpowered. Nonetheless, we found no signal of lower survival with COVID-19 infection with relative risk estimates essentially at the null value of 1.0. Third, data from 2021 is not available from GWTG-Resuscitation; therefore, our analysis of the association of COVID-19 infection and survival outcomes in children is limited to the initial pandemic variants during 2020. Finally, our results may not reflect the impact of the delta variant of COVID-19 on pediatric patients with a CPR event, as this COVID-19 variant affected more children, often with greater illness severity.

Conclusions

In a large multicenter national registry of CPR events, sCOVID-19 infection status was not associated with lower rates of ROSC or survival to hospital discharge in pediatric patients undergoing CPR.

Conflicts of Interest and Disclosures

- Dr. El-Zein is currently supported by the National Heart, Lung and Blood Institutes of Health under Award Number T32H110837. The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the National Institutes of Health.
- "The Get With The Guidelines® programs are provided by the American Heart Association." Hospitals participating in the registry submit clinical information regarding the medical history, hospital care, and outcomes of consecutive patients hospitalized for cardiac arrest using an online, interactive case report form and Patient Management Tool™ (IQVIA, Parsippany, New Jersey). IQVIA (Parsippany, New Jersey) serves as the data collection (through their Patient Management Tool – PMT) and coordination center for the American Heart Association/American Stroke Association Get With The Guidelines® programs. The University of Pennsylvania serves as the data analytic center and has an agreement to prepare the data for research purposes.

Contributors' statement

Rayan El-Zein and Paul S. Chan conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Maya L. Chan carried out the analyses. Lillian Su critically reviewed the manuscript.

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