Early Versus Late Advanced Airway Management for Pediatric Patients With Out-of-Hospital Cardiac Arrest

Shunsuke Amagasa, MD, PhD*; Shintaro Iwamoto, MAS; Masahiro Kashiura, MD; Hideto Yasuda, MD, PhD; Yuki Kishihara, MD; Satoko Uematsu, MD, PhD

*Corresponding Author. E-mail: amagasa0828@gmail.com.

Study objective: To determine the association between early versus late advanced airway management and improved outcomes in pediatric out-of-hospital cardiac arrest.

Methods: We performed a retrospective cohort study using data from the out-of-hospital cardiac arrest registry in Japan. We included pediatric patients (<18 years) with out-of-hospital cardiac arrest who had received advanced airway management (tracheal intubation, supraglottic airway, and esophageal obturator). The main exposure was early (≤20 minutes) versus late (>20 minutes) advanced airway management. The primary and secondary outcome measurements were survival and favorable neurologic outcomes at 1 month, respectively. To address resuscitation time bias, we performed risk-set matching analyses using time-dependent propensity scores.

Results: Out of the 864 pediatric patients with both out-of-hospital cardiac arrest and advanced airway management over 67 months (2014 to 2019), we included 667 patients with adequate data (77%). Of these 667 patients, advanced airway management was early for 354 (53%) and late for 313 (47%) patients. In the risk-set matching analysis, the risk of both survival (risk ratio 0.98 for early versus late [95% confidence interval 0.95 to 1.02]) and favorable 1-month neurologic outcomes (risk ratio 0.99 [95% confidence interval 0.97 to 1.00]) was similar between early and late advanced airway management groups. In sensitivity analyses, with time to early advanced airway management defined as ≤10 minutes and ≤30 minutes, both outcomes were again similar.

Conclusion: In pediatric out-of-hospital cardiac arrest, the timing of advanced airway management may not affect patient outcomes, but randomized controlled trials are needed to address this question further. [Ann Emerg Med. 2024;83:185-195.]

Please see page 186 for the Editor's Capsule Summary of this article.

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0196-0644/$-see front matter

https://doi.org/10.1016/j.annemergmed.2023.09.023

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INTRODUCTION

Background

Although out-of-hospital cardiac arrest is uncommon in children, it has high rates of morbidity and mortality.[1,2] The survival rate for pediatric cardiac arrest is consistently low, with published rates ranging from 2% to 22%, and has not improved in the last decade.[2-9]

Out-of-hospital cardiac arrest in children is usually secondary to respiratory failure, and advanced airway management is therefore suggested for all patients with out-of-hospital cardiac arrest. Advanced airway management includes endotracheal intubation and supraglottic airway.[7] Effective airway management is an important target for efforts to improve survival and recovery.[10]

Importance

Studies on pediatric out-of-hospital cardiac arrest have failed to find that advanced airway management benefits survival or recovery.[11-17] These studies are commonly limited, however, by a lack of time-based data and analysis. In particular, there are no studies on the effect of early versus late advanced airway management on pediatric out-of-hospital cardiac arrest. Clarifying the effect of early versus late advanced airway management is critical for determining the optimal airway management strategy for out-of-hospital cardiac arrest.

Goals of This Investigation

The objective of this study was to examine the association between the timing of advanced airway management in pediatric out-of-hospital cardiac arrest

Editor's Capsule Summary

What is already known on this topic

Although many studies favor advanced airway management in children with out-of-hospital cardiac arrest, the optimal timing remains unclear.

What question this study addressed

Does early (within 20 minutes of arrival) advanced airway management improve care compared to later efforts in children with out-of-hospital cardiac arrest?

What this study adds to our knowledge

In this observational study of a large sample from a national database in Japan, the timing of advanced airway management was not associated with improved patient outcomes.

How this is relevant to clinical practice

The efficiency and effectiveness of airway management may be more important than timing in out-of-hospital cardiac arrest.

and patient outcomes. We therefore performed a retrospective study using a national database in Japan, comparing patient outcomes between patients with early and late advanced airway management. We used risk-set matching with time-dependent propensity scores to control for resuscitation time bias. We hypothesized that early advanced airway placement would not be associated with improved outcomes.

METHODS

Study Design and Setting

This was a retrospective study of data from the Japanese Association for Acute Medicine Out-of-Hospital Cardiac Arrest (JAAM-OHCA) registry. The JAAM-OHCA registry is a national, multicenter, prospective project with targeted collection of out-of-hospital and inhospital data from Japanese patients with out-of-hospital cardiac arrest. The registry protocol was approved by each member's Institutional Review Board. The requirement for obtaining informed consent was waived. The current report was written in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Japanese Emergency Medical System

In Japan, Emergency Medical Service (EMS) systems are operated by local governments and overseen by the Japanese Fire and Disaster Management Agency.[17-19] All EMS staff are trained to perform cardiopulmonary resuscitation (CPR) in accordance with the guidelines developed by the Japan Resuscitation Council, which are based on the International Liaison Committee on Resuscitation statement.[20,21] Each EMS team consists of 3 EMS providers, including at least one emergency medical technician (EMT) with extensive training in out-of-hospital care. All EMTs are capable of using upper airway devices, such as laryngeal tubing and laryngeal masks. Only specially trained and certified EMTs, however, may perform tracheal intubations. These EMTs may intubate only if the patient is in cardiac arrest. Japanese EMS personnel are not legally authorized to terminate resuscitation in the field; all patients with out-of-hospital cardiac arrest are transported to the hospital unless death is certain and resuscitation efforts are not initiated.

Selection of Participants

We included patients aged <18 years from the JAAM-OHCA registry with documentation of advanced airway management during out-of-hospital cardiac arrest from June 2014 to December 2019. We excluded patients with missing data for key variables and outcomes of interest, patients with implausible times to advanced airway management (ie, negative values), and patients with a time to advanced airway management of 0 minutes or ≥60 minutes after EMS contact.

Measurements and Definitions

The source of all study data was the JAAM-OHCA registry, which combines out-of-hospital and inhospital data.[19] Out-of-hospital data were obtained from the Fire and Disaster Management Agency's All-Japan Utstein Registry.[18] Inhospital data were collected prospectively by physicians or medical staff at each institution using a report form. This database did not contain information regarding the type of inhospital advanced airway management. However, in Japan, an endotracheal tube is selected in most cases when advanced airway management is performed for cardiac arrest patients in hospitals.

For the current study, the following data were collected from the registry: (1) patient age and sex, (2) day of week, (3) witnessed arrest status, (4) bystander CPR, (5) initial monitored cardiac rhythm, (6) cause of cardiac arrest, (7) adrenaline administration, (8) shock delivery, (9) advanced airway placement, (10) presence of a physician during emergency transport, (11) presence of out-of-hospital advanced life support by a physician, (12) survival at 30 days after cardiac arrest, and (13) pediatric cerebral performance category at 30 days after cardiac arrest. Time data collected from the registry included the time of emergency call, EMS arrival, CPR started, arrival at the hospital, adrenaline administration (if given), shock delivery (if done), and advanced airway placement.

Days of week were classified as either weekdays or weekends. The time of emergency call was categorized as 7:00 to 14:59 hours, 15:00 to 22:59 hours, or 23:00 to 6:59 hours.[22] Witnessed arrest status was classified as none, EMS personnel, or others. Bystander CPR included rescue breathing. The initial monitored cardiac rhythm was defined as ventricular fibrillation, pulseless ventricular tachycardia, pulseless electrical activity, asystole, or others. The cause of cardiac arrest was classified as cardiogenic, respiratory, asphyxiation, traumatic, other intrinsic factors, or other extrinsic factors.

The main exposure of interest was early versus late advanced airway management during cardiac arrest. Advanced airway management was defined as tracheal intubation or placement of a supraglottic device or an esophageal obturator. "Early" advanced airway management was defined as ≤20 minutes and "late" advanced airway management as >20 minutes, both from the first EMS–patient contact. If the cardiac arrest was witnessed by EMS personnel, the times to advanced airway placement, adrenaline administration, and shock delivery were defined as the time from witnessing the cardiac arrest, not from EMS contact. We selected 20 minutes as the cutoff on the basis of a published study[23] and the feasibility of advanced airway placement in pediatric out-of-hospital cardiac arrest. Before analyses, we also examined the median and distribution of time to advanced airway placement to ensure that the 20-minute cutoff was reasonable.

The primary outcome was survival at 1 month after out-of-hospital cardiac arrest. The secondary outcome was any favorable neurologic outcome at 1 month. A "favorable" neurologic outcome was defined as a pediatric cerebral performance category of 1 to 3.[24] The pediatric cerebral performance category included the following 6 outcomes: (1) good cerebral recovery, (2) mild cerebral disability, (3) moderate cerebral disability, (4) severe cerebral disability, (5) coma or a vegetative state, and (6) death or brain death.

Statistical Analysis

We calculated standard descriptive statistics for exposure, outcomes, and other variables of interest. Categoric variables are presented as counts and percentages and continuous variables as medians and interquartile ranges (IQRs).

We analyzed the association between early versus late advanced airway management and patient outcomes using time-dependent propensity scores and risk-set matching. We used the Fine–Gray regression model with time-dependent covariates (eg, adrenaline administration or defibrillation), time-independent covariates (eg, patient age and bystander CPR), and competing risk events to produce propensity scores (all covariates listed in Table 1). We selected covariates primarily on the basis of their association with the exposure and/or outcomes in prior studies.[17,25-27] Propensity scores represent the likelihood of having early advanced airway management. Similar methods have been used in previous studies on the treatment of cardiac arrest and have been suggested to be effective in addressing resuscitation time bias.[17,25-27] Because we aimed to evaluate the efficacy of early advanced airway management, the Fine-Gary regression model considered the return of spontaneous circulation prior to advanced airway management as a competing risk and informative censoring.

Each patient with time to advanced airway management between 1 and 59 minutes following the first contact with EMS was matched with a patient at risk for but who had not yet received advanced airway management during the same time frame (risk-set matching). We computed the standardized differences for each covariate to assess the effectiveness of risk-set matching. A well-matched balance was defined as an absolute value of standardized difference of <0.20.[28]

We used the full matching method,[29,30] given that the number of pediatric patients with out-of-hospital cardiac arrest was relatively small. Full matching forms strata consisting of either one exposure subject and at least one control subject or one control subject and at least one exposure subject. Patients receiving advanced airway management were also considered patients at risk of receiving advanced airway management because the matching should not be predicated on future events. Although the matched controls were independent within the risk-set strata at each time point (minutes), several patients duplicated in the control group in the matched cohort for all strata combined; therefore, the number of cases for analysis might have been larger than the number of eligible cases. This was addressed by adjusting the frequency weighting to indicate the number of duplicates when analyzing the outcomes. In risk-set matching, pairs matched at the same time point were assumed to be correlated. Therefore, we used generalized estimating equations in the analysis of outcomes to estimate the risk ratio (RR) while taking within-pair correlation into account. The RR between the outcomes in early and late advanced airway management was estimated

Table 1. Characteristics of 667 pediatric patients with out-of-hospital cardiac arrest from the Japanese Association for Acute Medicine out-of-hospital cardiac arrest registry.

Characteristic	Early Advanced Airway Management (n=354)	Late Advanced Airway Management (n=313)	Standardized Difference
Age (y), median (IQR)	4 (0-14)	2 (0-13)	−0.217
Male, n (%)	220 (62.1)	194 (62.0)	0.003
Day of week, n (%)			0.118
Weekday	248 (70.1)	202 (64.5)	
Weekend	106 (29.9)	111 (35.5)	
Time of emergency call (hr), n (%)			0.016
7:00-14:59	128 (36.2)	115 (36.7)	
15:00-22:59	140 (39.5)	124 (39.6)	
23:00-6:59	86 (24.3)	74 (23.6)	
Tertiles of prefecture performance rates of out-of-hospital advanced airway management, n (%)			0.717
Low tertile (0%-12.5%)	70 (19.8)	157 (50.2)	
Middle tertile (12.6%-15.5%)	166 (46.9)	113 (36.1)	
High tertile (15.6%-)	118 (33.3)	43 (13.7)	
Witness status, n (%)			0.267
None	242 (68.4)	219 (70.0)	
EMS personnel	28 (7.9)	7 (2.2)	
Others	84 (23.7)	87 (27.8)	
Bystander CPR, n (%)			0.066
Presence	158 (44.6)	137 (43.8)	
Absence	154 (43.5)	132 (42.2)	
Presence including rescue breathing	42 (11.9)	44 (14.1)	
Initial monitored cardiac rhythm, n (%)			0.182
VF	12 (3.4)	11 (3.5)	
Pulseless VT	1 (0.3)	2 (0.6)	
PEA	66 (18.6)	50 (16.0)	
Asystole	262 (74.0)	246 (78.6)	
Other	13 (3.7)	4 (1.3)	
Cause of cardiac arrest, n (%)			0.39
Cardiogenic	80 (22.6)	110 (35.1)	
Respiratory	14 (4.0)	16 (5.1)	
Asphyxiation	15 (4.2)	25 (8.0)	
Traumatic	81 (22.9)	43 (13.7)	
Other intrinsic*	83 (23.4)	66 (21.1)	
Other extrinsic†	81 (22.9)	53 (16.9)	
Time from emergency call to start of CPR, median min (IQR)	9 (7-11)	8 (7-10)	−0.147
Time from the patient contact by EMS to arrival at the hospital, median min (IQR)	18 (13-27)	22 (17-28)	0.137
Adrenaline administration before advanced airway management, n (%)	61 (17.2)	52 (16.6)	0.016
Time from the patient contact by EMS to adrenaline administration before advanced airway management, median min (IQR)	14 (12-16)	17.5 (15-19)	0.898
Shock delivery before advanced airway management, n (%)	15 (4.2)	19 (6.1)	0.083

Table 1. Continued.

Characteristic	Early Advanced Airway Management (n=354)	Late Advanced Airway Management (n=313)	Standardized Difference
Time from the patient contact by EMS to shock delivery before advanced airway management, median min (IQR)	3 (1-4.5)	4 (1-7)	0.403
Out-of-hospital advanced airway management, n (%)	114 (32.2)	4 (1.3)	0.910
Out-of-hospital advanced airway management type, n (%)			0.97
Laryngeal mask	15 (4.2)	0	
Esophageal obturator	88 (24.9)	3 (1.0)	
Endotracheal tube	20 (5.6)	1 (0.3)	
Physician during emergency transport, n (%)	62 (17.5)	24 (7.7)	0.300
Out-of-hospital advanced life support by physician, n (%)	88 (24.9)	46 (14.7)	0.257

CPR, cardiopulmonary resuscitation; *EMS*, emergency medicine service; *IQR*, interquartile range; *PEA*, pulseless electrical activity; *VF*, ventricular fibrillation; *VT*, ventricular tachycardia.
*Cerebrovascular disease, malignancy, sudden infant death syndrome, or others.
†Suicide by hanging, drowning, poisoning, or unknown extrinsic.

using generalized estimating equations with modified Poisson regression with robust variance.

In Japan, CPR training and procedures are based on the International Resuscitation Liaison Committee consensus guidelines[20] and are standardized according to the Japanese guidelines for pulmonary resuscitation,[21] so there are few regional differences. However, some regions have age restrictions for out-of-hospital advanced airway placement. Therefore, to adjust for regional differences, we divided prefectures into tertiles on the basis of the rate of advanced airway management and used these tertiles to calculate propensity scores as in the prior studies.[17]

All tests were 2 sided, and a P value of <.05 was considered statistically significant. All analyses were conducted using R software, version 4.1.3 (www.r-project.org).

Sensitivity Analysis

We performed 3 predetermined sensitivity analyses (Tables E1 to E3 [available at http://www.annemergmed.com]). We repeated our main analysis of early versus late advanced airway management with both ≤10 minutes and ≤30 minutes as alternative cutoffs for early and late advanced airway management, respectively. We also performed a time-dependent propensity score matching analysis using nearest neighbor matching, which was also used in previous studies.[17,25] Additionally, a time-dependent propensity score matching analysis was performed using a Cox regression model that did not account for competing risks to estimate the time-dependent propensity score.[31,32]

RESULTS

Enrollment

Altogether, 51,199 patients were enrolled in the JAAM-OHCA registry during the period of interest (Figure). Among the 1,064 patients aged <18 years, 864 had documentation of advanced airway management. From this group, we excluded a total of 197 patients—147 with missing data on time to advanced airway management, 23 with a time to advanced airway management of 0 or ≥60 minutes, 20 with missing data for other variables of interest, 5 with the return of spontaneous circulation prior to EMS contact, and 2 with implausible time data (negative values). Thus, our study sample consisted of 667 patients aged <18 years with out-of-hospital cardiac arrest (77% of patients with advanced airway management).

Table E4 (available at http://www.annemergmed.com) presents the characteristics of cases excluded due to no advanced airway management and missing data on time to advanced airway management. The no advanced airway management group had a lower rate of bystander CPR, a higher rate of cardiogenic cause of cardiac arrest, and a higher rate of classification of the initial monitored cardiac rhythm as other compared with the eligible patients. No other notable characteristics were identified among the available characteristics.

Patient Characteristics

Among the 667 patients, 354 (53.1%) had early advanced airway management and 313 (46.9%) had late advanced airway management (Table 1). Compared with

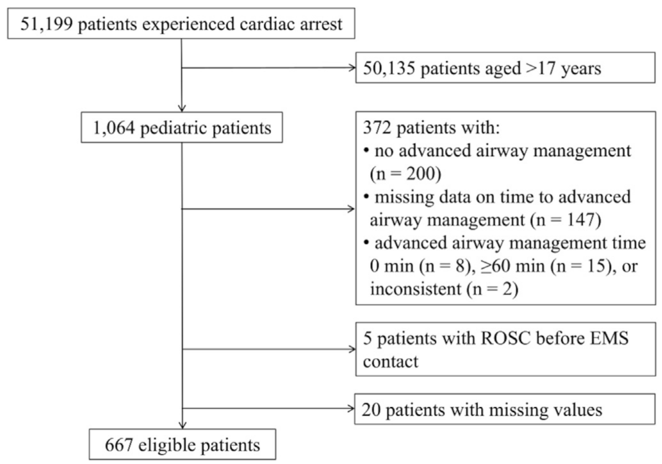

Figure. Study flowchart. *EMS*, emergency medical service; *ROSC*, return of spontaneous circulation.

patients with late advanced airway management, patients with early advanced airway management were older (median 4 years [IQR 0, 14] versus median 2 years [IQR 0, 13]), more likely to have EMS witness arrest (early 7.9%, late 2.2%), and more likely to be with a physician during emergency transport (early 17.5%, late 7.7%).

Regarding inhospital treatment, 11 (3.1%) and 8 (2.6%) patients in the early and late advanced airway management groups, respectively, received extracorporeal membrane oxygenation, and 29 (8.2%) and 28 (8.9%) patients received target temperature management, respectively.

Main Results

Among the 667 eligible patients, 54 (8.1%) survived until 1 month after cardiac arrest and 19 (2.8%) had a favorable neurologic outcome at 1 month after cardiac arrest (Table 2). Seven-hundred eight patients were matched using time-dependent propensity scores. The standardized differences were <0.20 for all variables except one (time from EMS contact to adrenaline administration before advanced airway management), indicating well balance after matching (Table 3).

In the main analysis, the RR of survival with early advanced airway management was 0.98 (95% confidence interval [CI] 0.95 to 1.02; Table 4). The RR of favorable neurologic outcomes at 1 month with early advanced airway management was 0.99 (95% CI 0.97 to 1.00). In the sensitivity analysis, the results were similar for both survival (≤10 minutes with early versus late RR 0.97 [95% CI 0.89 to 1.06] and ≤30 minutes RR 1.00 [95% CI 0.93 to 1.08]) and favorable neurologic outcomes (≤10 minutes RR 0.99 [95% CI 0.96 to 1.02] and ≤30 minutes RR 1.00 [95% CI 0.98 to 1.01]).

Additionally, in the time-dependent propensity score matching analysis using nearest neighbor matching (Table E2) and the time-dependent propensity score matching analysis using a Cox regression model, there were no significant differences in survival or favorable neurologic outcomes between early and late advanced airway management in most of the analyses (Tables E2, E3, and E5). Additional study methods and results of sensitivity analyses and subgroup analyses are provided in the Supplemental Methods and Results (Appendix E1, available at http://www.annemergmed.com).

LIMITATIONS

The current study has several limitations. First, in a propensity-matched study, there is a risk of residual confounding, especially with time-dependent interventions and outcomes. Moreover, the study has a relatively small sample size, and the number of cases was small for some variables. We attempted to mitigate the risk of residual confounding by including a large number of variables and by using full matching. We performed full matching in the main analysis to limit sample size reduction and the exclusion of patients with outcome occurrences that did not have a match. However, the number of cases changed significantly during the matching process for variables that were only present in a small number of cases. Second, as in any study of out-of-hospital cardiac arrest, the number

Table 2. Outcomes of the original and time-dependent propensity score–matched cohorts.

Outcome	No. of Patients With Outcomes: Early Advanced Airway Management	Late Advanced Airway Management
Original cohort	n=354	n=313
Survival at 1 month after cardiac arrest (%)	27 (7.6)	27 (8.6)
Favorable neurologic outcomes at 1 month after cardiac arrest (%)	10 (2.8)	9 (2.9)
Time-dependent propensity score–matched cohort	n=354	n=354
Survival at 1 month after cardiac arrest (%)	27 (7.6)	18 (5.1)
Favorable neurologic outcomes at 1 month after cardiac arrest (%)	10 (2.8)	5 (1.4)

Table 3. Demographics and characteristics of the time-dependent propensity score–matched cohort.

Characteristic	Early Advanced Airway Management (n=354)	Late Advanced Airway Management (n=354)	Standardized Difference
Age (y), median (IQR)	4 (0-14)	3 (0-14)	−0.05
Male, n (%)	220 (62.1)	226 (63.8)	0.035
Day of week, n (%)			0.031
Weekday	248 (70.1)	243 (68.6)	
Weekend	106 (29.9)	111 (31.4)	
Time of emergency call (hr), n (%)			0.135
7:00-14:59	128 (36.2)	115 (32.5)	
15:00-22:59	140 (39.5)	140 (39.5)	
23:00-6:59	86 (24.3)	86 (24.3)	
Tertiles of prefecture performance rates of out-of-hospital advanced airway management, n (%)			0.068
Low tertile (0%-12.5%)	70 (19.8)	61 (17.2)	
Middle tertile (12.6%-15.5%)	166 (46.9)	174 (49.2)	
High tertile (15.6%)	118 (33.3)	119 (33.6)	
Witness status, n (%)			0.112
None	242 (68.4)	260 (73.4)	
EMS personnel	28 (7.9)	24 (6.8)	
Others	84 (23.7)	70 (19.8)	
Bystander CPR, n (%)			0.085
Presence	158 (44.6)	171 (48.3)	
Absence	154 (43.5)	148 (41.8)	
Presence including rescue breathing	42 (11.9)	35 (9.9)	
Initial monitored cardiac rhythm, n (%)			0.107
VF	12 (3.4)	9 (2.5)	
Pulseless VT	1 (0.3)	1 (0.3)	
PEA	66 (18.6)	62 (17.5)	
Asystole	262 (74.0)	274 (77.4)	
Other	13 (3.7)	8 (2.3)	
Cause of cardiac arrest, n (%)			0.121
Cardiogenic	80 (22.6)	76 (21.5)	
Respiratory	14 (4.0)	15 (4.2)	
Asphyxiation	15 (4.2)	8 (2.3)	
Traumatic	81 (22.9)	86 (24.3)	
Other intrinsic*	83 (23.4)	88 (24.9)	
Other extrinsic†	81 (22.9)	81 (22.9)	
Time from emergency call to start of CPR, median min (IQR)	9 (7-11)	9 (7-11)	0.007
Time from the patient contact by EMS to arrival at the hospital, median min (IQR)	18 (13-27)	21 (16-28)	0.06
Adrenaline administration before advanced airway management, n (%)	61 (17.2)	61 (17.2)	0
Time from the patient contact by EMS to adrenaline administration before advanced airway management, median min (IQR)‡	14 (12-16)	16 (13-18)	0.65

Table 3. Continued.

Characteristic	Early Advanced Airway Management (n=354)	Late Advanced Airway Management (n=354)	Standardized Difference
Shock delivery before advanced airway management, n (%)	15 (4.2)	14 (4.0)	0.014
Time from the patient contact by EMS to shock delivery before advanced airway management, median min (IQR) ‡	3 (1-4.5)	3.5 (1-7.5)	0.417
Out-of-hospital advanced airway management, n (%)	114 (32.2)	111 (31.4)	0.018
Out-of-hospital advanced airway management type, n (%)			0.05
Laryngeal mask	15 (4.2)	17 (4.8)	
Esophageal obturator	88 (24.9)	82 (23.2)	
Endotracheal tube	20 (5.6)	22 (6.2)	
Physician during emergency transport, n (%)	62 (17.5)	57 (16.1)	0.038
Out-of-hospital advanced life support by physician, n (%)	88 (24.9)	80 (22.6)	0.053

*Cerebrovascular disease, malignancy, sudden infant death syndrome, or others.
†Suicide by hanging, drowning, poisoning, or unknown extrinsic.
‡Because the variable is only for patients who received that treatment, matching does not necessarily improve the balance.

of patients with survival or favorable outcomes was relatively small. Thus, the power of the study might have been insufficient to detect differences in the main outcomes. Third, the patients in our study were more likely to receive advanced airway management with supraglottic airway in the out-of-hospital setting, particularly in the early advanced airway management group, which may affect both residual confounding and the generalizability of our results. However, several studies have suggested that differences between the use of endotracheal intubation and supraglottic airway in the out-of-hospital setting are not associated with outcomes.[12,15,33] Additionally, in this study, physicians were sometimes part of the out-of-hospital team, more often in the early group than in the late group. This may also affect generalizability. Finally, the 200 patients who did not receive advanced airway management were excluded. Therefore, the results can only be extrapolated to patients with out-of-hospital cardiac arrest who receive any advanced airway management. Additionally, 147 cases with advanced airway management were excluded due to missing time data. Given the relatively smaller sample size,

Table 4. Outcomes between early and late advanced airway management in risk-set matching using time-dependent propensity scores.

	No. of Patients With Outcomes		
Outcome	Early Advanced Airway Management	Late Advanced Airway Management	RR (95% CI)
Early advanced airway management defined as ≤20 min			
Survival at 1 month after cardiac arrest (%)	27/354 (7.6)	18/354 (5.1)	0.98 (0.95-1.02)
Favorable neurologic outcomes at 1 month after cardiac arrest (%)	10/354 (2.8)	5/354 (1.4)	0.99 (0.97-1.00)
Sensitivity analysis			
Early advanced airway management defined as ≤10 min			
Survival at 1 month after cardiac arrest (%)	12/130 (9.2)	8/130 (6.2)	0.97 (0.89-1.06)
Favorable neurologic outcomes at 1 month after cardiac arrest (%)	6/130 (4.6)	6/130 (4.6)	1.00 (0.93-1.08)
Early advanced airway management defined as ≤30 min			
Survival at 1 month after cardiac arrest (%)	47/564 (8.3)	27/564 (4.8)	0.99 (0.96-1.02)
Favorable neurologic outcomes at 1 month after cardiac arrest (%)	15/564 (2.7)	11/564 (2.0)	1.00 (0.98-1.01)

CI, confidence interval; *RR*, risk ratio.

the inclusion of these patients might have affected the main analysis.

DISCUSSION

One of the major problems when considering interventions during CPR is resuscitation time bias, a type of systematic error/immortal time bias,[34] indicating that the comparatively poorer prognosis group with longer CPR times is more likely to receive interventions such as advanced airway management. Because longer resuscitation times for cardiac arrest result in worse outcomes, interventions will be biased toward poor outcomes if the resuscitation time bias is not approached. Recently, risk-set matching with time-dependent propensity scores has been reported to be effective in addressing resuscitation time bias.[25,31,32] However, studies on advanced airway management in pediatric out-of-hospital cardiac arrest addressing resuscitation time bias have only compared whether out-of-hospital advanced airway management was or was not performed.[17] Intubation may ultimately be necessary in the case of cardiopulmonary arrest; therefore, the issue at hand is not simply whether to intubate, but rather the timing of when to do so.[35]

In a propensity-matched study of children with out-of-hospital cardiac arrest in the JAAM-OHCA registry, we found no differences in survival or favorable neurologic outcomes between early and late advanced airway management. In contrast, a prior observational study of 761 pediatric patients in Japan with out-of-hospital cardiac arrest found that earlier out-of-hospital advanced airway management was associated with improved outcomes.[23] Three other studies—2 observational on adults with out-of-hospital cardiac arrest (Japan) and a secondary analysis of the Resuscitation Outcomes Consortium Prehospital Resuscitation using an Impedance Valve and Early versus Delayed study (United States and Canada)—also found early advanced airway management to be associated with neurologic outcomes.[36-38]

Although early advanced airway management was associated with better outcomes in these studies, resuscitation time bias might have influenced these results. As noted, patients with later advanced airway management tend to have longer resuscitation times than those with earlier advanced airway management.[34] Therefore, in observational studies on out-of-hospital cardiac arrest, it is essential to account for resuscitation time bias when examining the effectiveness of treatments during resuscitation. Similar to our study, an observational study on out-of-hospital advanced airway management in 3,801 pediatric patients with out-of-hospital cardiac arrest addressed resuscitation time bias using risk-set matching with time-dependent propensity scores.[17] This study also found no association between out-of-hospital advanced airway management and survival or favorable neurologic outcomes. In addition, a secondary analysis of 2,146 adult out-of-hospital cardiac arrest patients enrolled in the Pragmatic Airway Resuscitation Trial used risk-set matching with a time-dependent propensity score and also found that the timing of advanced airway management was not associated with survival to hospital discharge.[27]

In pediatric patients with out-of-hospital cardiac arrest, the results of our study and the available pediatric evidence suggest that advanced airway placement may not necessarily be a priority early in resuscitation. Our study and the existing literature have significant limitations, however, and cardiac arrest patients are highly heterogeneous. Hence, there is a possibility of effect modification, with early advanced airway management being effective in certain patient subgroups. Given the state of the literature on airway management in pediatric patients with out-of-hospital cardiac arrest, a multicenter, randomized, controlled trial is clearly needed to further address the question of early versus late advanced airway management. Effective randomization eliminates concerns of residual confounding. Sample sizes would need to be large, with the study power based on published rates of survival and favorable neurologic outcomes. A multicenter design and collaboration between out-of-hospital, emergency department, and hospital groups would both be essential to the study's success. Subgroup analyses could also be planned to determine whether specific patient groups benefit from early airway management. A clinical trial would also need rigorous inclusion criteria and to have appropriate methodology to ensure the accurate collection of time-based variables.

In summary, in an observational study of pediatric out-of-hospital cardiac arrest in Japan, we found no evidence that early advanced airway placement was associated with improved survival or neurologic outcomes at 1 month after cardiac arrest.

Supervising editor: Benjamin T. Kerrey, MD, MS. Specific detailed information about possible conflict of interest for individual editors is available at https://www.annemergmed.com/editors.

Author affiliations: From the Department of Emergency and Transport Medicine (Amagasa, Uematsu), National Center for Child Health and Development, Setagaya-ku, Tokyo, Japan; the Department of Data Science (Iwamoto), Clinical Research Center, National Center for Child Health and Development, Setagaya-ku, Tokyo, Japan; and the Department of Emergency and Critical Care

Medicine (Kashiura, Yasuda, Kishihara), Saitama Medical Center, Jichi Medical University, Saitama City, Saitama, Japan.

Author contributions: SA, MK, HY, and YK conceptualized the study. SA and SI designed the study. SI contributed to analysis. SA and SI contributed to data interpretation. SA drafted the article. SI, MK, HY, YK, and SU critically revised the article for important intellectual content. All authors have read and approved the final version of the article. SA takes responsibility for the paper as a whole.

Data sharing statement: The data underlying this article were provided by the JAAM by permission. Data will be shared on request to the corresponding author with permission of the JAAM.

Authorship: All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: By *Annals'* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist. The authors report this article did not receive any outside funding or support.

Publication dates: Received for publication April 18, 2023. Revisions received June 24, 2023, and September 25, 2023. Accepted for publication September 28, 2023.

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