RESUSCITATION 137 (2019) 161–167

Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

Relationship between institutional case volume and one-month survival among cases of paediatric out-of-hospital cardiac arrest

Shunsuke Amagasa[a,b,*], Masahiro Kashiura[a], Takashi Moriya[a], Satoko Uematsu[b], Naoki Shimizu[c], Atsushi Sakurai[d], Nobuya Kitamura[e], Takashi Tagami[f], Munekazu Takeda[g], Yasufumi Miyake[h], on behalf of the SOS-KANTO 2012 Study Group

[a] Department of Emergency and Critical Care Medicine, Saitama Medical Center, Jichi Medical University, 1-847, Amanuma-cho, Omiya-ku, Saitama City, Saitama, 330-8503, Japan
[b] Division of Emergency and Transport Services, National Center for Child Health and Development, 2-10-1, Okura, Setagaya-ku, Tokyo, 157-8535, Japan
[c] Department of Critical Care and Emergency Medicine, Tokyo Metropolitan Children's Medical Center, 2-8-29, Musashidai, Fuchu, Tokyo, 183-8561, Japan
[d] Division of Emergency and Critical Care Medicine, Department of Acute Medicine, Nihon University School of Medicine, 30-1, Oyagutikamichou, Itabashi-ku, Tokyo, 173-8610, Japan
[e] Department of Emergency and Critical Care Medicine, Kimitsu Chuo Hospital, 1010, Sakurai, Kisarazushi, Chiba, 292-8535, Japan
[f] Department of Emergency and Critical Care Medicine, Nippon Medical School Tama Nagayama Hospital, 1-7-1, Nagayama, Tama-shi, Tokyo, 206-8512, Japan
[g] Department of Critical Care and Emergency Medicine, Tokyo Women's Medical University, 8-1, Kawada-cho, Shinjuku-ku, Tokyo, 162-8666, Japan
[h] Department of Emergency Medicine, Teikyo University School of Medicine, 2-11-1 Kaga, Itabashi-Ku, Tokyo, 173-8606, Japan

Abstract

Aim: To evaluate volume–outcome relationship in paediatric out-of-hospital cardiac arrest (OHCA).

Methods: This *post hoc* analysis of the SOS-KANTO 2012 study included data of paediatric OHCA patients <18 years old who were transported to the 53 emergency hospitals in the Kanto region of Japan between January 2012 and March 2013. Based on the paediatric OHCA case volume, the higher one-third of institutions (more than 10 paediatric OHCA cases during the study period) were defined as high-volume centres, the middle one-third institutions (6–10 cases) were defined as middle-volume centres and the lower one-third of institutions (less than 6 cases) were defined as low-volume centres. The primary outcome measurement was survival at 1 month after cardiac arrest. Multivariate logistic regression analysis for 1-month survival and paediatric OHCA case volume were performed after adjusting for multiple propensity scores. To estimate the multiple propensity score, we fitted a multinomial logistic regression model, which fell into one of the three groups as patient demographics and prehospital factors.

* Corresponding author at: Department of Emergency and Critical Care Medicine, Saitama Medical Center, Jichi Medical University, 1-847, Amanuma-cho, Omiya-ku, Saitama City, Saitama, 330-8503, Japan.
E-mail address: amagasa0828@gmail.com (S. Amagasa).

https://doi.org/10.1016/j.resuscitation.2019.02.021
Received 17 September 2018; Received in revised form 11 February 2019; Accepted 12 February 2019

Results: Among the eligible 282 children, 112, 82 and 88 patients were transported to the low-volume (36 institutions), middle-volume (11 institutions) and high-volume (6 institutions) centres, respectively. Transport to a high-volume centre was significantly associated with a better 1-month survival after adjusting for multiple propensity score (adjusted odds ratio, 2.55; 95% confidence interval, 1.05–6.17).

Conclusion: There may be a relationship between institutional case volume and survival outcomes in paediatric OHCA.

Keywords: Volume–outcome relationship, Children, Emergency medical services, Cardiopulmonary resuscitation, Patient outcome assessment

Introduction

Out-of-hospital cardiac arrest (OHCA) is uncommon in children, with a rate of 2–9 cases per 100,000 children per year.[1–5] Although there are several guidelines for paediatric cardiac arrest such as the Paediatric Advanced Life Support by the American Heart Association, outcomes of OHCA are poor, with survival rates ranging from 2% to 22%.[1–6] Therefore, improvement of survival rates in paediatric OHCA cases, which has been limited over the last decades,[5,7] is an important issue.

High-quality, specialised medical approaches are required for children experiencing a critical illness or severe trauma and those requiring certain surgeries, and centralisation of such cases at children's hospitals were previously reported to be associated with improved outcomes.[8–13] In addition, some studies reported that children's hospitals led to improved outcomes in children with in-hospital cardiac arrest and OHCA.[1,14,15] However, due to the lack of children's hospitals in certain areas, not all children with OHCA might be transported initially to a children's hospital. Although several studies reported that high-volume centres were associated with better OHCA outcomes in adults,[16–20] few studies examined the volume–outcome relationship in paediatric OHCA, and the effect of paediatric volume alone on outcomes in these cases remains unclear. A better understanding of the volume–outcome relationship in paediatric OHCA may aid in constructing an efficient emergency transport system and improving care and outcome of paediatric OHCA patients.

We hypothesised that a high volume is associated with better outcomes for paediatric OHCA. To evaluate our hypothesis, we investigated the volume–outcome relationship in paediatric OHCA.

Methods

Study design and setting

The current study was a *post hoc* analysis of the data from the SOS-KANTO 2012 study.[21–23] The SOS-KANTO 2012 was a prospective multicentre study of patients with OHCA who were transported to emergency hospitals in the Kanto area of Japan. The study was conducted between January 2012 and March 2013. The design and data collection methods used in the SOS-KANTO 2012 study were previously reported in detail.[21–23] The Kanto area consists primarily of urban areas including Tokyo. Two of the 67 hospitals that participated in the study were children's hospital. The present study was approved by the relevant institutional review boards of all participant institutions. The review boards waived the need for written informed consent to ensure participant anonymity.

In Japan, the emergency medical service (EMS) system is operated by each municipal government and is supervised by the Fire and Disaster Management Agency of Japan. All EMS personnel are trained to perform cardiopulmonary resuscitation (CPR) according to the Japanese resuscitation guidelines produced by the Japan Resuscitation Council based on a statement from the International Liaison Committee on Resuscitation. EMS personnel generally select an institution to which they can transport the patient in the shortest time from among institutions according to the severity of the patient. For paediatric OHCA patients, EMS personnel generally consider the nearest critical care center for acceptance of the patient. However, they occasionally bypass the nearest critical care center based on communication between the EMS personnel and the physician. EMS personnel in Japan are not legally permitted to terminate resuscitation in the field, and all OHCA patients are transported to hospitals, except in cases where death is certain.

Patients

All OHCA patients transported to the participant hospitals by EMS personnel were included in the SOS-KANTO 2012 study. The current study included paediatric OHCA patients $<$18 years of age who were enrolled in the SOS-KANTO 2012 study. Patients with missing data for primary outcomes were excluded.

Data collection

The EMS personnel collected prehospital information based on the Utstein-style template, including age, sex, witnessed cardiac arrest, bystander CPR, time interval, initial rhythm monitored and prehospital management and event. Physicians collected data on in-hospital treatments and outcomes, including the survival and neurological outcomes at 1 month after cardiac arrest, as well as determined the aetiology of cardiac arrest.[21–23]

Measurements and definitions

The primary outcome measurement was survival at 1 month after cardiac arrest, as per several landmark previous studies.[1,15,16,24,25]

Hospital volume was defined as the number of eligible patients treated at each hospital and it was subcategorized into tertiles, as per previous studies.[17,18,24] The cut-off value was defined to trisect the number of patients as equally as possible. The higher one-third of institutions (more than 10 paediatric OHCA cases during the study period) were defined as high-volume centres, the middle one-third institutions (6–10 cases) were defined as middle-volume centres and the lower one-third of institutions (less than 6 cases) were defined as low-volume centres. Cardiac arrest was defined as the absence of mechanical cardiac activity, as determined by the absence of pulse and normal breathing, while OHCA was defined as cardiac arrest that occurred out of the hospital.[21,22] Activity of daily living (ADL) was classified into good, moderate impairment, severe impairment and vegetative state. Arrest location was classified into private residence and others. Initial cardiac rhythm was classified into ventricular tachycardia (VT)/ventricular fibrillation (VF) and pulseless electrical activity (PEA)/asystole/others. Aetiology was classified into cardiogenic, traumatic and others. Period of time of the emergency call was classified into 7:00–14:59 h, 15:00–22:59 h and 23:00–6:59 h, as per our previous study.[26]

Statistical analysis

We compared demographic factors, patient characteristics, care in the hospital and the outcomes among the patients transported to the high-volume, middle-volume and low-volume centres. Trends of discrete variables among three groups were analysed using the Mantel–Haenszel trend test, and continuous variables were analysed using ANOVA.

To minimise bias and maximise the analyses power, we undertook multiple imputation to account for missing data.[27] Five multiply imputed datasets were generated, and multivariate logistic regression analyses were performed to evaluate the association between paediatric OHCA case volume and survival at 1 month after cardiac arrest to each dataset. Estimates were then combined.

Because the rate of occurrence of the event (survival at 1 month) was expected to be low, we used multiple propensity score analysis in multivariate analysis to avoid a problem of overfitting.[28,29] A propensity score represents the conditional probability of a particular exposure, given a set of measured baseline covariates, and is an established method for reducing confounding factors in observational studies. Although propensity score matching or stratification has commonly been used to assemble similar patient cohorts in terms of baseline covariates for 2-group comparisons,[30] a multiple propensity score approach has been used for comparisons of three or more groups.[31] A multiple propensity score is defined as the conditional probability of being categorized into a particular group of 3 or more, given a set of observed baseline covariates. To estimate the multiple propensity score for the current analysis, we fitted a multinomial logistic regression model, which fell into one of the three groups, as patient demographics and prehospital factors, including age,[7,32] sex,[7,32,33] ADL, cardiac arrest location,[4,7] witnessed cardiac arrest,[3,4,7] bystander CPR,[3,4,7] initial cardiac rhythm,[3,4,7] aetiology (cardiogenic, traumatic and others),[1,3,4] period of time of the emergency call,[26] CPR, shock delivery,[3,34] adrenaline administration,[3,4,34,35] airway management[36,37] and advanced airway management[3,4,34,35] by EMS personnel, ROSC before the EMS personnel reached the patient,[38,39] ROSC during transportation,[38,39] time from the emergency call to reaching the patient[3,4,38,39] and time from departure from the scene to arrival at the hospital.[3,4,38,39] Next, we used multivariate logistic regression to analyse the association between paediatric OHCA case volume and survival at 1 month after the cardiac arrest with an adjustment for multiple propensity scores.

All statistical tests were two sided, and an α level of 0.05 was considered to indicate significance. All data analyses were performed using the SPSS statistical software package version 24 (IBM, New York, USA).

Results

Patients

A total of 16,452 patients with cardiac arrest were enrolled in the SOS-KANTO 2012 study, including 288 patients aged <18 years (Fig. 1). After the exclusion of 6 cases with missing data of primary outcome, 282 patients were included in the final analyses, including 112, 82 and 88 patients who were transported to the low-volume (36 institutions), middle-volume (11 institutions) and high-volume (6 institutions) centres, respectively. Patients aged <18 years had not been transported to 14 of 67 participant hospitals during the study period.

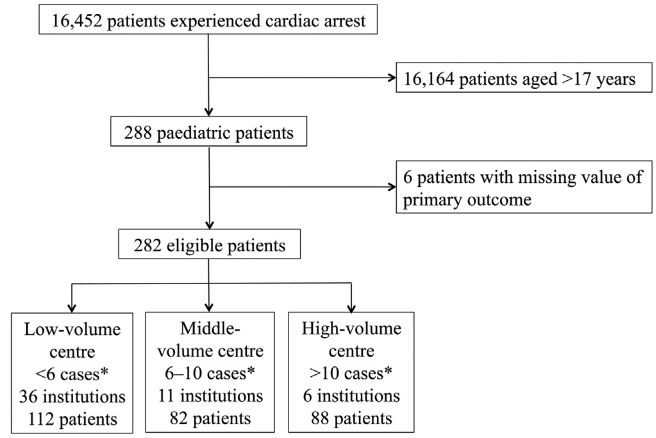

Fig. 1 – Flowchart of the study.
***During study period (1 year and 3 months).**

Demographics and prehospital characteristics of the study population

The age of patients in low-volume centres was significantly higher compared with that in the other two groups (Table 1). The time from departure from the scene to arrival at the hospital was significantly longer for high-volume centres than for the low-volume centres.

The deference of in-hospital care and outcome among institutions

The in-hospital cares among institutions were not significantly different (Table 2). With regard to the outcomes, high-volume centre showed a significant tendency of better survival rate after 1 month of cardiac arrest (Table 3). Although the neurological outcomes in high volume centre were better than those in the other two groups, the difference was not statistically significant.

Multivariate logistic regression analyses for 1 month survival adjusted by multiple propensity score

We found that high-volume centre (adjusted odds ratio [OR], 2.55; 95% confidence interval, 1.05–6.17) was significantly associated with a better 1-month survival rate compared with low-volume centres (Table 4).

Discussion

The present study retrospectively reviewed the data of the SOS-KANTO 2012, a multicentre observational study, and evaluated the volume–outcome relationship of paediatric OHCA. We found that a higher frequency of paediatric OHCA cases were associated with better survival rate after multiple propensity score analysis adjusted for measured confounding factors. Because there was no major difference in ADL prior to arrest, the number of patients who were not qualified to receive advanced life support and in-hospital care among the institutions, we speculated that the outcome was due to the quality of care in the emergency department and the intensive care unit. This important finding may aid in constructing the emergency transport system for paediatric OHCA cases and identifying approaches to improve care for children with OHCA.

Table 1 – The demographics and prehospital characteristics of study population.

	Low-volume centre (n = 112, 36 institutions)	Middle-volume centre (n = 82, 11 institutions)	High-volume centre (n = 88, 6 institutions)	*p*
Number of patients per institution, median (IQR)	3 (2–5)	8 (7–8)	12.5 (12–17.5)	<0.001
Age, median (IQR)	3 (0–13)	1 (0–10)	2 (0–9)	<0.001
Age <1 year, n (%)	40 (35.7)	39 (47.6)	35 (39.8)	0.50
Female, n (%)	43 (38.4)	39 (47.6)	36 (40.9)	0.66
ADL				0.70
Good, n (%)	81 (85.3)	52 (81.3)	68 (87.2)	
Moderate impairment, n (%)	4 (4.2)	3 (4.7)	3 (3.8)	
Severe impairment, n (%)	9 (9.5)	8 (12.5)	7 (9.0)	
Vegetative state, n (%)	1 (1.1)	1 (1.6)	0	
Arrest location (private residence), n (%)	74 (66.7)	53 (67.1)	64 (72.7)	0.37
Witnessed cardiac arrest, n (%)	54 (48.2)	38 (46.3)	33 (37.5)	0.14
Bystander CPR, n (%)	53 (47.3)	33 (40.2)	38 (43.2)	0.53
Initial rhythm (VT/VF), n (%)	2 (1.8)	5 (6.2)	5 (5.7)	0.16
Aetiology				0.052
Cardiogenic, n (%)	19 (18.1)	17 (21.8)	27 (31.0)	
Traumatic, n (%)	20 (19.0)	14 (17.9)	16 (18.4)	
Others, n (%)	66 (62.9)	47 (60.3)	44 (50.6)	
Period of time				0.57
7:00–14:59, n (%)	38 (33.9)	32 (39.0)	38 (43.2)	
15:00–22:59, n (%)	41 (36.6)	31 (37.8)	25 (28.4)	
23:00–6:59, n (%)	33 (29.5)	19 (23.2)	25 (28.4)	
ROSC before the EMS personnel reached the patient, n (%)	4 (3.8)	0	6 (7.3)	0.27
ROSC during transportation				0.37
ROSC, n (%)	3 (2.7)	3 (3.7)	5 (5.9)	
Temporal, n (%)	1 (0.9)	1 (1.2)	1 (1.2)	
CPR by EMS personnel, n (%)	99 (88.4)	76 (92.7)	74 (84.1)	0.52
Shock delivery by EMS personnel, n (%)	3 (2.7)	7 (9.1)	7 (8.3)	0.10
Adrenaline administration by EMS personnel, n (%)	1 (1.0)	4 (5.3)	5 (6.0)	0.06
Airway management by EMS personnel, n (%)	97 (87.4)	73 (92.4)	78 (91.8)	0.26
Advanced airway management by EMS personnel, n (%)	13 (12.5)	11 (14.3)	15 (19.2)	0.27
Time from the emergency call to reaching the patient, median min (IQR)	8 (6–11)	8 (7–10)	9 (7–12)	0.07
Time from departure from the scene to arrival at the hospital, median min (IQR)	10 (6–13)	9.5 (6–14)	10 (7–16)	0.03

IQR, interquartile range; ADL, activity of daily living; CPR, cardio pulmonary resuscitation; VT, ventricular tachycardia; VF, ventricular fibrillation; ROSC, return to spontaneous circulation; EMS, emergency medicine service.
Proportions exclude missing data.

Table 2 – The deference of in-hospital care among institutions.

	Low-volume centre (n = 112, 36 institutions)	Middle-volume centre (n = 82, 11 institutions)	High-volume centre (n = 88, 6 institutions)	*p*
Advanced life support, n (%)	97 (86.6)	75 (91.5)	75 (86.8)	0.59
Intubation, n (%)	85 (75.9)	63 (76.8)	66 (75.0)	0.90
Adrenaline administration, n (%)	90 (80.3)	66 (80.5)	61 (69.3)	0.08
Renal replacement therapy, n (%)	0	1 (1.2)	1 (1.1)	0.32
Extracorporeal membrane oxygenation, n (%)	1 (0.9)	2 (2.4)	0	0.60
Target temperature management, n (%)	6 (5.5)	8 (9.8)	14 (15.9)	0.14

Table 3 – The deference of outcome among institutions.

	Low-volume centre (n = 112, 36 institutions)	Middle-volume centre (n = 82, 11 institutions)	High-volume centre (n = 88, 6 institutions)	*p*
Survival at 1 month after cardiac arrest, n (%)	10 (8.9)	14 (17.1)	18 (20.5)	0.02
PCPC at 1 month after cardiac arrest ≤ 3, n (%)	6 (5.4)	4 (4.9)	11 (12.5)	0.07

PCPC, Paediatric cerebral performance category.[40].

Table 4 – Multivariate logistic regression analyses for 1 month survival adjusted by multiple propensity score.

	adjusted OR (95% CI)	*p*
Institution		
Low-volume centre	Reference	
Middle-volume centre	1.99 (0.80–4.97)	0.14
High-volume centre	2.55 (1.05–6.17)	0.038

A multiple propensity score is defined as the conditional probability of falling into a particular group of three groups of institutional OHCA volume. We fitted a multinomial logistic regression model, which fell into one of the three groups as patient demographics and prehospital factors.

The volume–outcome relationship in paediatric OHCA is still a matter of debate. Many studies described that a high volume of cases with cardiac arrest had a good impact on outcomes in adults.[16–20] In the nationwide study of Korea, the survival rate to hospital discharge for adults with OHCA was significantly higher at high-volume centres than in low-volume centres even when transportation times were longer.[16] A recent prospective study described that a high frequency of post-cardiac arrest treatment was an independent predictor for favourable outcomes.[17] The volume–outcome relationship in adults with OHCA was also observed in a nationwide study of the United States[18] and a systematic review.[19] In contrast, several studies reported that there was no significant association between the OHCA volume and the outcome in children and adults.[24,25] These studies described that the case volume for healthcare providers was a more likely predictor of survival than hospital volume. Among adults, the volume–outcome relationship in OHCA was evaluated, and the prevailing opinion is that increasing OHCA volume improves the outcome. However, there are few studies regarding the volume–outcome relationship of paediatric OHCA, and the association between case volumes and outcome remains unclear.

In the present study, we observed gradual improvement of survival rate at one month after cardiac arrest among low-volume (reference), middle-volume (OR 1.99) and high-volume (OR 2.55) centres, and the difference in outcome between high- and low-volume centres was statistically significant. To minimise bias, maximise the analyses power and avoid problems of overfitting, multiple imputation to address missing data and multiple propensity score analysis were undertaken, allowing adjustment of many confounding factors. We found the volume–outcome relationship in the analyses after multiple propensity score analysis, adjusting for measured patient characteristics, prehospital factors and treatments. There are few studies on volume–outcome relationship for OHCA that adjust for these many factors.

With regard to institutional volume of the current study, 288 children were transported to 53 institutions over the course of 1 year and 3 months, with an average of 4.35 children per institution per year. In a nationwide study conducted in the United States that compared the outcome of paediatric OHCA between paediatric and general emergency departments, an average of 4.83 children with OHCA were transported to one institution per year.[1] The case volume per institution in the current study was comparable with this earlier study. Because of differences in the EMS system between Japan and other countries, our results cannot be generalizable for other countries. However, paediatric OHCA case volumes per institution in Japan may be similar to that in other countries, and our results may be applicable to other regions.

Although there are few studies on the efficacy of OHCA volume on outcomes in children, several studies examined the association between hospital characteristics and outcome in children with cardiac arrest. In a nationwide sample in the United States, survival from paediatric nontraumatic OHCA to hospital discharge was higher in paediatric emergency departments than in general emergency departments.[1] Another study described that teaching hospitals where paediatric-trained physicians were present were associated with improved survival of children with in-hospital cardiac arrest.[14,15] Additionally, centralisation of care for children with critical illnesses or severe trauma and those requiring certain surgeries improved outcomes in these patients, because ongoing training and education are critical to maintain and improve the high level of skill needed.[8–13] Because of the specific needs of the children, care of less common critical cases such as cardiac arrest may require proficiency. The results from these previous studies on paediatric specialization were consistent with our results. Therefore, there may be an influence of paediatric OHCA volume on outcomes.

The current study has several limitations. First, the current study included data from institutions from a limited area. We could not investigate the differences in urbanisation. The Kanto area where the current study was conducted consists primarily of urban areas, including the capital city, Tokyo. In the future, an analysis of the urbanisation level in a large, nationwide study is necessary. Second, the number of eligible paediatric cases and the rate of occurrence of the event to the number of potential confounding factors were relatively low. To avoid problems of overfitting, multivariate analyses adjusted by multiple propensity score were undertaken in this study. However, the OHCA population was extremely heterogeneous in the present study. While we attempted to adjust many variables using multiple propensity analysis, the small numbers of patients involved is a limitation of this analysis. Third, although we used multiple propensity score and adjusted the measured confounding factors, the problem of unmeasured confounding factors still remained. For example, information about transfer to children's hospital was not included. In addition, our data did not contain detailed information on the underlying disease. Instead, we obtained data on ADL prior to cardiac arrest and multiple propensity score analysis included the factor of ADL. Fourth, the current study could not perform multivariate analysis of the neurological outcomes and examine long-term outcomes. Future prospective studies including neurological and long-term outcomes are necessary to further examine the volume–outcome relationship in paediatric OHCA.

Conclusions

In the present study, paediatric OHCA case volume was associated with survival at 1 month after cardiac arrest. There may be a relationship between institutional case volume and survival outcomes in paediatric OHCA. Further investigation of the volume–outcome relationship of paediatric OHCA in large-scale studies is required.

Conflicts of interest

None.

Acknowledgements

This study was supported by Japanese Association for Acute Medicine of Kanto. The funder had no role in the execution of this study or interpretation of the results. All members that participated in the current study are the member of Japanese Association for Acute Medicine of Kanto. We declare that we have no financial conflict of interest. SOS-KANTO 2012 steering council and study group was shown in Supplementary data.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.02.021.

REFERENCES

1. Michelson KA, Hudgins JD, Monuteaux MC, Bachur RG, Finkelstein JA. Cardiac arrest survival in pediatric and general emergency departments. Pediatrics 2018;141:e20172741.
2. Bardai A, Berdowski J, van der Werf C, et al. Incidence, causes, and outcomes of out-of-hospital cardiac arrest in children. A comprehensive, prospective, population-based study in the Netherlands. J Am Coll Cardiol 2011;57:1822–8.
3. Tham LP, Wah W, Phillips R, et al. Epidemiology and outcome of paediatric out-of-hospital cardiac arrests: a paediatric sub-study of the Pan-Asian resuscitation outcomes study (PAROS). Resuscitation 2018;125:111–7.
4. Nehme Z, Namachivayam S, Forrest A, Butt W, Bernard S, Smith K. Trends in the incidence and outcome of paediatric out-of-hospital cardiac arrest: a 17-year observational study. Resuscitation 2018;128:43–50.
5. Fink EL, Prince DK, Kaltman JR, et al. Resuscitation outcomes consortium. Unchanged pediatric out-of-hospital cardiac arrest incidence and survival rates with regional variation in North America. Resuscitation 2016;107:121–8.
6. Gerein RB, Osmond MH, Stiell IG, Nesbitt LP, Burns S, OPALS Study Group. What are the etiology and epidemiology of out-of-hospital pediatric cardiopulmonary arrest in Ontario, Canada? Acad Emerg Med 2006;13:653–8.
7. Jayaram N, McNally B, Tang F, Chan PS. Survival after out-of-hospital cardiac arrest in children. J Am Heart Assoc 2015;4: e002122.
8. Pearson G, Schann F, Barry P, et al. Should paediatric intensive care be centralized? Trent versus Victoria. Lancet 1997;349:1213–7.
9. Tilford JM, Simpson PM, Green JW, Lensing S, Fiser DH. Volume-outcome relationships in pediatric intensive care units. Pediatrics 2000;106:289–94.
10. Goy AY, Mok Q. Centralization of paediatric intensive care: are critically ill children appropriately referred to a regional centre? Intensive care Med 2001;27:730–5.
11. Marcin JP, Song J, Leigh JP. The impact of pediatric intensive care unit volume on mortality: a hierarchical instrumental variable analysis. Pediatr Crit Care Med 2005;6:136–41.
12. Hall JR, Reyes HM, Meller JL, Loeff DS, Dembek R. The outcome for children with blunt trauma is best at a pediatric trauma center. J Pediatr Surg 1996;31:72–6.
13. Kalfa D, Chai P, Bacha E. Surgical volume-to-outcome relationship and monitoring of technical performance in pediatric cardiac surgery. Pediatric Cardiol 2014;35:899–905.
14. Donoghue AJ, Nadkarni VM, Elliott M, Durbin D, American Heart Assocation National Registry of Cardiopulmonary Resuscitation Investigators. Effect of hospital characteristics on outcomes from pediatric cardiopulmonary resuscitation: a report from the national registry of cardiopulmonary resuscitation. Pediatrics 2006;118:995–1001.
15. Hansen M, Fleischman R, Meckler G, Newgard CD. The association between hospital type and mortality among critically ill children in US EDs. Resuscitation 2013;84:488–91.
16. Cha WC, Lee SC, Shin SD, Song KJ, Sung AJ, Hwang SS. Regionalisation of out-of-hospital cardiac arrest care for patients without prehospital return of spontaneous circulation. Resuscitation 2012;83:1338–42.
17. Schober A, Sterz F, Laggner AN, et al. Admission of out-of-hospital cardiac arrest victims to a high volume cardiac arrest center is linked to improved outcome. Resuscitation 2016;106:42–8.
18. Carr BG, Goyal M, Band RA, et al. A national analysis of the relationship between hospital factors and post-cardiac arrest mortality. Intensive Care Med 2009;35:505–11.
19. Nguyen YL, Wallace DJ, Yordanov Y, et al. The volume outcome relationship in critical care: a systematic review and meta-analysis. Chest 2015;148:79–92.
20. Spaite DW, Bobrow BJ, Stolz U, et al. Statewide regionalization of postarrest care for out-of-hospital cardiac arrest: association with survival and neurologic outcome. Ann Emerg Med 2014;64:496–506.
21. SOS-KANTO 2012 Study Group. Changes in pre- and in-hospital management and outcomes for out-of-hospital cardiac arrest between 2002 and 2012 in Kanto, Japan: the SOS-KANTO 2012 Study. Acute Med Surg 2015;2:225–33.
22. Sos-Kanto 2012 Study Group. Changes in treatments and outcomes among elderly patients with out-of-hospital cardiac arrest between 2002 and 2012: a post hoc analysis of the SOS-KANTO 2002 and 2012. Resuscitation 2015;97:76–82.
23. Tanaka C, Kuno M, Yokota H, et al. Changes in atropine use for out-of-hospital cardiac arrest patients with non-shockable rhythm between 2002 and 2012. Resuscitation 2016;101:e5–6.
24. Cudnik MT, Sasson C, Rea TD, et al. Increasing hospital volume is not associated with improved survival in out of hospital cardiac arrest of cardiac etiology. Resuscitation 2012;83:862–8.
25. Sakai-Bizmark R, Friedlander SMI, Marr EH, Mena LA, Corral I, Chang RR. Patient characteristics and emergency department factors associated with survival after sudden cardiac arrest in children and young adults: a cross-sectional analysis of a nationally representative sample, 2006–2013. Pediatr Cardiol 2018;39:1216–28.
26. Matsumura Y, Nakada T, Shinozaki K, et al. Nighttime is associated with decreased survival and resuscitation efforts for out-ofhospital cardiac arrests: a prospective observational study. Crit Care 2016;20:141.
27. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009;338:b2393.
28. Feng P, Zhou XH, Zou QM, Fan MY, Li XS. Generalized propensity score for estimating the average treatment effect of multiple treatments. Stat Med 2012;31:681–97.
29. Spreeuwenberg MD, Bartak A, Croon MA, et al. The multiple propensity score as control for bias in the comparison of more than two treatment arms: an introduction from a case study in mental health. Med Care 2010;48:166–74.
30. Hagihara A, Hasegawa M, Abe T, Nagata T, Wakata Y, Miyazaki S. Prehospital epinephrine use and survival among patients with out-of-hospital cardiac arrest. JAMA 2012;307:1161–8.
31. Bangalore S, Pencina MJ, Kleiman NS, Cohen DJ. Prognostic implications of procedural vs spontaneous myocardial infarction: results from the Evaluation of Drug Eluting Stents and Ischemic Events (EVENT) registry. Am Heart J 2013;166:1027–34.
32. Goto Y, Maeda T, Goto Y. Impact of dispatcher-assisted bystander cardiopulmonary resuscitation on neurological outcomes in children with out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. J Am Heart Assoc 2014;3:e000499.
33. Meert KL, Telford R, Holubkov R, et al. Therapeutic Hypothermia after Pediatric Cardiac Arrest (THAPCA) Trial Investigators. Pediatric out-

of-hospital cardiac arrest characteristics and their association with survival and neurobehavioral outcome. Pediatr Crit Care Med 2016;17:e543–50.
34. Tijssen JA, Prince DK, Morrison LJ, et al. Time on the scene and interventions are associated with improved survival in pediatric out-of-hospital cardiac arrest. Resuscitation 2015;94:1–7.
35. Andersen LW, Berg KM, Saindon BZ, et al. Time to epinephrine and survival after pediatric in-hospital cardiac arrest. JAMA 2015;314:802–10.
36. Hansen ML, Lin A, Eriksson C, et al. A comparison of pediatric airway management techniques during out-of-hospital cardiac arrest using the CARES database. Resuscitation 2017;120: 51–6.
37. Hansen M, Lambert W, Guise JM, Warden CR, Mann NC, Wang H. Out-of-hospital pediatric airway management in the United States. Resuscitation 2015;90:104–10.
38. Goto Y, Maeda T, Nakatsu-Goto Y. Decision tree model for predicting long-term outcomes in children with out-of-hospital cardiac arrest: a nationwide, population-based observational study. Crit Care 2014;18: R133.
39. Atkins DL, Everson-Stewart S, Sears GK, et al. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest. Circulation 2000;119:1484–9.
40. Fiser DH. Assessing the outcome of pediatric intensive care. J Pediatr 1992;121:68–74.