Outcomes of paediatric out-of-hospital cardiac arrest according to hospital characteristic defined by the annual number of paediatric patients with invasive mechanical ventilation: a nationwide study in Japan

Running Title

Relationship between hospital characteristic and outcomes of paediatric out-of-hospital cardiac arrest

Author

Takahiro Kido[1,2], Masao Iwagami[2,3], Hideo Yasunaga[4], Toshikazu Abe[2,3,5], Yuki Enomoto[1,6], Hiroki Matsui[4], Kiyohide Fushimi[7], Hidetoshi Takada[1,8], Nanako Tamiya[2,3]

1) Department of Pediatrics, University of Tsukuba Hospital, Ibaraki, Japan
2) Department of Health Services Research, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan
3) Health Services Research and Development Center, University of Tsukuba, Ibaraki, Japan
4) Department of Clinical Epidemiology and Health Economics, School of Public Health, The University of Tokyo, Japan
5) Department of General Medicine, Juntendo University, Tokyo, Japan
6) Department of Critical Care and Emergency medicine, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan
7) Department of Health Policy and Informatics, Tokyo Medical and Dental University Graduate School of Medicine, Tokyo, Japan
8) Department of Child Health, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan

Corresponding author:
Masao Iwagami, MD, MPH, MSc, PhD
Department of Health Services Research, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, Japan
Telephone: +81 (0)29 853 8849
Fax: +81 (0)29 853 8849
Email: iwagami-tky@umin.ac.jp

Abstract

Aim: We examined whether outcomes of paediatric out-of-hospital cardiac arrest (OHCA) are associated with a hospital characteristic defined by the annual number of invasive mechanical ventilation cases, suggesting hospitals' experience in caring for severely ill paediatric patients.

Method: We analysed the Japanese Diagnosis Procedure Combination database from 2010 to 2017. We identified children (<18 years) with OHCA and post-resuscitation intensive care (defined as invasive mechanical ventilation and/or catecholamine infusion). Hospitals were divided into four groups by mean annual number of paediatric cases involving invasive mechanical ventilation. The primary outcome was in-hospital mortality, and the secondary outcome was unfavourable outcomes (death or medical care dependency at discharge). Multivariable logistic regression analyses were conducted to examine the relationship between hospitals' experience and outcomes.

Results: We included 2,540 paediatric OHCA patients from 385 institutions. Overall in-hospital mortality was 62.4%, with rates of 69.6%, 61.3%, 61.8%, and 57.0% in hospitals with low (≤48 cases/year), low-intermediate (48–110), high-intermediate (110–164), and high (>164) experience levels ($P < .001$), respectively. Compared to hospitals with low experience, adjusted odds ratios (95% confidence interval) for hospitals with low-intermediate, high-intermediate, and high experience were as follows: primary outcome: 0.64 (0.40–1.01), 0.67 (0.42–1.05), and 0.46 (0.31–0.70), respectively; secondary outcome: 0.93 (0.55–1.57), 0.95 (0.63–1.43), and 0.67 (0.46–0.96), respectively.

Conclusion: Japanese hospitals with higher experience in caring for severely ill paediatric patients showed lower mortality for paediatric OHCA. This fact should be considered by the Emergency Medical Systems when deciding transport strategy.

Keywords: children; cardiopulmonary resuscitation; mechanical ventilation; out-of-hospital cardiac arrest; volume-outcome relationship

Introduction

Despite current progress in healthcare system, the survival rate following paediatric out-of-hospital cardiac arrest (OHCA) is low at approximately 15%.[1,2] Recent studies have shown that new treatment strategies, such as extracorporeal membrane oxygenation (ECMO), targeted temperature management (TTM), and early coronary intervention, could improve outcomes in adults.[3,4] However, because of its rarity and unusual pathophysiology, the most effective strategy for paediatric OHCA treatment remains unclear.[5, 6]

The relationship between hospital volume (the average number of patients with the disease of interest in each hospital) and patient outcomes has been widely examined in surgical and acute-care settings.[7] Some previous studies show that the mortality rate for adult OHCA patients transferred to high-volume institutions was lower than that of those in low-volume institutions; this probably occurred because high-volume institutions are well equipped and experienced.[8,9, 10, 11, 12, 13] However, in paediatric intensive care units, evidence demonstrating a relationship between hospital volume and patient outcomes is scarce.[14, 15,16] Because the rarity of paediatric OHCA, many hospitals experience few or no cases annually. Therefore, hospital volume could be an unsuitable indicator of staff proficiency or equipment in the management of paediatric OHCA. A recent Japanese study suggested that institutional paediatric OHCA case volume was associated with 1-month survival after cardiac arrest.[17] However, the study included only large emergency hospitals in a limited area in Japan, which restricted the generalisability of the results.

We expected the number of paediatric cases involving invasive mechanical ventilation to be a useful index of the management of paediatric OHCA patients (i.e. measuring the ‘experience’ of each hospital), because paediatric invasive mechanical ventilation is a highly skilled procedure and potentially reflects hospitals’ capability to care for severely ill paediatric patients. In addition, the number of paediatric patients using invasive mechanical ventilation is generally much higher relative to that of paediatric OHCA patients. We hypothesised that hospitals with high experience levels (measured as the average annual number of paediatric cases involving invasive mechanical ventilation) would produce superior outcomes for paediatric OHCA patients. To test this hypothesis, we conducted a retrospective cohort study using a Japanese national inpatient claims database.

Method

Data source

We used The Japanese Diagnosis Procedure Combination (DPC) database.[18] Briefly, the database includes hospital discharge abstract and administrative claims data from more than 1,000 voluntarily participating hospitals in Japan. Large hospitals are more likely to submit data to the database: all 82 academic hospitals and over 90% of tertiary care emergency hospitals contribute, and more than 400,000 paediatric patients are enrolled each year.[19] The dataset includes hospital identification number, hospital academic status, patient demographic characteristics, admission and discharge dates, main and comorbid diagnoses at admission, and complications during hospitalisation (which were coded according to the International Classification of Diseases [ICD-10]), discharge status, procedure or operation dates and codes (in Japanese), and prescribed medicines. Physicians attended to patient records to establish diagnoses at discharge.

Because the anonymous nature of the data, informed consent was waived when the study was approved by the Institutional Review Board at the University of Tokyo.

Study population

In the DPC database for the 2010 to 2017 fiscal years, we identified children younger than 18 years old who were admitted through the emergency room with an admission diagnosis of

ICD-10 code I46.0 (cardiac arrest with successful resuscitation), I46.1 (sudden cardiac death), I46.9 (cardiac arrest, unspecified), I49.0 (ventricular fibrillation), or I47.2 (ventricular tachycardia), and performed post-resuscitation intensive care (defined as invasive mechanical ventilation or catecholamine infusion) after admission. In-hospital cardiac arrest (IHCA) was not included.

We excluded patients who were transferred to another hospital within 2 days of admission or transferred from other hospitals to the current hospital. Further, we excluded patients who were admitted to neonatal intensive care units, died in the emergency room, were admitted to hospitals that did not participate in the DPC database continuously between 2010 and 2017, and who had missing zip code data.

Exposure and outcome

The exposure of interest in this study was a hospital characteristic, defined as the mean annual number of paediatric cases involving invasive mechanical ventilation, as a proxy for hospitals' experience in caring for severely ill paediatric patients. According to previous research,[19] we divided the studied hospitals into four categories (low, low-intermediate, high-intermediate, and high experience levels), with equal numbers of patients in each category.

The primary outcome was in-hospital mortality, and the secondary outcome was unfavourable discharge status defined as either death or new-onset medical care dependency at discharge. We regarded patients as dependent on medical care if any type of respiratory support (including oxygenation, non-invasive positive pressure ventilation, and nasal high-flow therapy) or tube feeding (via nasogastric tube or gastrostomy) was provided on the day of discharge.

Covariates

The following covariates were extracted as potential confounding factors in the association between hospitals' experience and outcomes: hospital characteristics including academic status (university hospital or other) and board-certified status in emergency care; patient characteristics including age, sex, year of hospitalisation, diagnosis of comorbidities (trauma, congenital heart disease, or congenital anomaly other than congenital heart disease) at admission, and procedures performed during hospitalisation (invasive mechanical ventilation, catecholamine infusion, TTM, ECMO, and continuous hemodiafiltration).

In addition, we calculated the distance between patients' homes and the hospitals to which they were transferred, as the best available proxy for transfer distance in the current dataset. The zip code centroids for patients' homes and destination hospitals were ascertained via decimal longitude and latitude degrees. The ellipsoidal distance was then calculated between the two points along the surface of a mathematical model of the earth based on the World Geodetic System, 1984 datum. We acknowledged that paediatric OHCA could have occurred at a location distant from patients' homes. However, a previous study suggested that most paediatric OHCA occurred at home, with a concordance rate of 83.5%.[20] In addition, considering that most children's daily lives (e.g. going to school) revolve around their homes in Japan, the distance between their homes and hospitals could be a good proxy for transfer distance for the purpose of confounding-variable adjustment.

Statistical analysis

We presented patient and hospital characteristics for the four groups according to hospitals' experience levels (low, low-intermediate, high-intermediate, and high). Continuous variables are presented as medians and interquartile range (IQR), and categorical variables are presented as numbers and proportions. To assess the trends for the characteristic within the four categories, we conducted Cuzick's test for non-parametric continuous variables and

Cochrane-Armitage test for categorical variables.

We estimated in-hospital mortality overall and by the four groups and determined whether in-hospital mortality tended to be increased (or decreased) according to hospitals' experience, using the Cochrane-Armitage test. We then performed a multivariable logistic regression analysis to examine the independent association between the four groups and in-hospital mortality, taking account of clustering by hospital using robust standard errors. We adjusted for the aforementioned covariates (i.e. academic and emergency centre certification of hospitals; patient characteristics including age, sex, year of hospitalisation, transport distance, diagnosis of comorbidities at admission; and procedures performed during hospitalisation). We repeated the analyses for the secondary outcome.

To examine the robustness of our analysis, we conducted several additional analyses. First, we conducted a stratified analysis by age group: infants (age <1), toddler (≧1, <6) and school age (≧6, <18). Second, we conducted subgroup analysis in patients with and without a diagnosis of ventricular fibrillation or ventricular tachycardia (Vf/VT) at admission. This was because previous studies suggested that, of the wide variety of underlying causes of OHCA, Vf/VT showed clearly better outcomes [1,21] Third, we restricted the analysis to patients without congenital heart disease. Finally, for potential concern that the selection of cut-off point in defining the hospital category could change the conclusion, we conducted sensitivity analyses by (i) dividing the studied hospitals into three categories (instead of four), and (ii) regarding the exposure (i.e. mean annual number of paediatric cases involving invasive mechanical ventilation) as a continuous variable in the multivariable logistic regression analysis.

All tests were two tailed, and p values of < .05 were considered statistically significant. All analyses were performed using STATA version 15 (StataCorp, Texas, USA).

Results

In total, 7,074 paediatric patients were admitted to 656 institutions with cardiac-arrest-related diagnoses between 2010 and 2017 (**Figure 1**). The median paediatric OHCA case load in each institution was 5 (IQR: 2–17) during the 8-year study period. Of note, 150 and 372 institutions had treated only one case and fewer than eight cases of paediatric OHCA during this period (i.e. less than one case per year), respectively. After we applied the exclusion criteria, 2,540 patients from 385 institutions, including 624 patients in hospitals with low experience (0–48 paediatric cases with invasive mechanical ventilation/year), 626 patients in hospitals with low-intermediate experience (48–101 cases/year), 651 patients in hospitals with high-intermediate experience (101–164 cases/year), and 639 patients in hospitals with high experience levels (>164 cases/year), were ultimately included in the analysis. Patients admitted to hospitals with more experience were younger, more likely to travel further to hospital from home, have been diagnosed congenital disease with or without cardiac defect, and less likely to have trauma, relative to patients admitted to hospitals with less experience (**Table 1**).

The number and proportion of primary and secondary outcomes by hospital category are shown in **Figure 2**. The in-hospital mortality was 62.4% (1,584/2,540) overall, and it tended to be lower in hospitals with higher experience levels (P for trend <.001). The incidence of the secondary outcome was 68.5% (1,739/2,540) overall, and it tended to be lower in hospitals with higher experience levels (P for trend <.001).

Compared to hospitals with low experience, unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) for in-hospital mortality were 0.94 (0.78–1.37), 0.97 (0.80–1.16), and 0.74 (0.62–0.89) for hospitals with low-intermediate, high-intermediate, and high experience levels, respectively (**Table 2**). After adjusting for covariates, adjusted ORs (95% CI) for in-hospital mortality were 0.63 (0.40–1.01), 0.67 (0.42–1.05), and 0.46 (0.31–0.70) for hospitals with low-intermediate, high-intermediate, and high experience levels, respectively.

The adjusted ORs (95% CI) for the secondary outcome were 0.93 (0.55–1.57), 0.95 (0.63–1.43), and 0.67 (0.46–0.96) for hospitals with low-intermediate, high-intermediate, and high experience levels, respectively (**Table 3**).

In stratified analysis by age group, similar trends to the main analysis were observed (**Table 4**). In the subgroup analysis of patients without a Vf/VT diagnosis, the result was consistent with the main analysis (**Supplement Table 1**). We were unable to conduct a multivariable regression analysis of patients with Vf/VT, because of the small sample size and number of outcomes; the in-hospital mortality rate for patients with a diagnosis of VF/VT was 7.4% (31/417). Exclusion of a small number of patients without congenital heart disease showed similar results (**Supplement Table 2**). When we divided the studied hospitals into three categories; low (<66 paediatric cases with invasive mechanical ventilation/year), intermediate (>=66, <137), and high (>=137) experienced group, the results showed a similar trend (**Supplement Table 3**). When we regarded the exposure (i.e. mean annual number of paediatric cases involving invasive mechanical ventilation) as a continuous variable, the adjusted OR (95%CI) per 100 cases/year increase was 0.85 (0.78-0.94).

Discussion

To our knowledge, this is the first study to examine the relationship between hospitals' capability to provide intensive care for paediatric patients and in-hospital outcomes for paediatric OHCA. The results showed that hospitals with high experience levels showed lower in-hospital mortality rates, relative to those in hospitals with low experience levels, for paediatric OHCA patients in post-resuscitation management.

The overall in-hospital mortality rate (following admittance and initiation of intensive care) was 64.6%. Although data regarding outcomes for paediatric OHCA are limited, previous studies conducted in the UK and Australia reported that the intra-paediatric intensive care unit mortality rate following paediatric OHCA was 50%.[22, 23] The difference in adjusted ORs for in-hospital mortality between the hospitals with high and low experience levels was remarkable. Though not statistically significant, mortality rates in the middle two groups (i.e. hospitals with high-intermediate and low-intermediate experience) were also lower relative to those with low levels of experience. These trends were consistent with our hypothesis.

Most previous studies examining adult OHCA reported that patients admitted to high-volume hospitals showed better outcomes, relative to those observed in low-volume hospitals,[3, 9, 10, 8, 13] while one study showed the opposite.[11] Moreover, only one study has examined paediatric OHCA and reported that the paediatric OHCA case load in each institution was associated with 1-month survival following cardiac arrest.[17] The study used data from voluntarily participating, large emergency hospitals within a limited area consisting of primary urban areas. However, the incidence of paediatric OHCA is rare, and grouping them by frequency is impractical. Indeed, results of our study showed that more than half (372/656) of hospitals providing OHCA treatment had encountered one or no cases annually. Thus, a widely adaptable indicator for quality of care in resuscitated OHCA children has not yet been proposed.

Invasive mechanical ventilation is the most frequently used and fundamental procedure in intensive care. A previous article reported that the number of patients undergoing invasive mechanical ventilation in hospital was associated with improved outcomes. [19] Patients with unstable respiratory, haemodynamic, or neurological conditions following resuscitation after OHCA require respiratory care provided by highly qualified medical professionals, in addition to specific post-cardiac arrest care including TTM and ECMO. Thus, we expected the annual number of paediatric cases involving invasive mechanical ventilation to reflect the quality of paediatric intensive care and be associated with OHCA outcomes in children. The results of this study suggest that, when a child was resuscitated from OHCA and require intensive care afterwards, those admitted to hospital with larger cases of paediatric invasive mechanical ventilation (>164 cases/year, approximating >1 case every 2 days) could have better outcomes than those admitted to hospitals with fewer cases (0–48 cases/year, approximating <1 case per week). A previous study reported that outcomes following paediatric IHCA were not associated with various hospital-volume parameters including the number of invasive mechanical ventilation cases.[24] Moreover, in IHCA, the incidence rate and underlying conditions could interact with other hospital characteristics.

The development of resuscitation centres has been discussed in previous articles,[25, 26] some of which suggested that direct transportation of adult patients with OHCA to resuscitation centres or facilities with high levels of relevant experience improved patient outcomes. [9,10, 27,28] The integration of patients could aid in the maintenance of the quality of resuscitation, standardized post-resuscitation care in adults, and the same could be said for the paediatric population. The centralisation of paediatric OHCA in children's hospitals could be a suitable means of achieving this: staff and equipment at these hospitals are well suited to paediatric resuscitation and intensive care. A previous study reported that paediatric admission to children's hospitals improved outcomes for in-hospital cardiac arrest and OHCA.[29, 30] Because the effectiveness of resuscitation centres could vary between disease categories, healthcare systems, and landscapes, studies examining paediatric OHCA in each region are required.

The study was subject to several limitations. First, this observational study suggested just an association, which does not necessarily mean causation. Next, although it included most large and acute-care hospitals in Japan, they were not selected randomly from all Japanese hospitals. Therefore, the generalisability of the findings to hospitals that do not submit data to the database is limited. Furthermore, the results are not extrapolatable to other countries with different health systems. In addition, the selection of the study participants was based on ICD-10 codes I46.0 (cardiac arrest with successful resuscitation), I46.1 (sudden cardiac death), I46.9 (cardiac arrest, unspecified), I49.0 (ventricular fibrillation), and I47.2 (ventricular tachycardia) as admission diagnoses. However, misclassification of diagnoses could have occurred when attending physicians coded the diagnoses. A previous validation study examining DPC data demonstrated high specificity (exceeding 96%) for several diagnoses[31], but the validity of cardiac arrest-related diagnoses is unknown. Furthermore, misclassification of transport distance could have occurred, because we calculated the distance between patients' home and the hospitals as the best available proxy for transport distance. Moreover, there could have been residual or unmeasured confounding factors affecting the association between the hospital category and paediatric OHCA outcomes. Although we have adjusted for year of hospitalisation, there may be residual confounding associated with potential changes on post-CPR quality along the years. The DPC does not contain pre-hospital or pre-resuscitation information (except for VF/VT diagnosis and the distance between patients' home address and hospitals), such as witness of cardiac arrest, paramedic response time for CPR, quality and duration of CPR, and doses of adrenaline,[1, 32] although we do not believe that these factors are largely imbalanced between the hospitals (as the pre-hospital care for OHCA is provided by the ambulance crew and they are educated by uniform curriculum in Japan). In addition, the severity assessment scales, such as the Paediatric Index of Mortality 2/3, were not adjusted for in the multivariable analysis. However, we restricted the study population to patients receiving catecholamine infusion or invasive mechanical ventilation at admission, to ensure a certain level of severity, allowing fair comparison between hospitals. Finally, this study only tested whether the current best available (easily measurable) hospital characteristic that we proposed was associated with outcomes of paediatric OHCA. There may be better indicators suggestive of hospital's capability for paediatric OHCA than the annual number of paediatric patients with invasive mechanical ventilation. Further studies are warranted to establish hospital indicators associated with outcomes of paediatric out-of-hospital cardiac arrest.

Conclusion

Using a Japanese national database, this study highlighted the association between hospital category classified according to the number of invasively mechanically ventilated children with paediatric OHCA outcomes. In Japan, children admitted to ‘high complexity’ hospitals after OHCA had better outcomes than those admitted to ‘low level’ hospitals. This fact should be considered by the Emergency Medical Systems in order to decide the transport strategy.

Funding sources

None.

Conflicts of Interest

HY received grants from Ministry of Health, Labour, and Welfare, Japan, during the conduct of the study. The other authors have nothing to declare.

Acknowledgments

We are grateful to the editor in Editage for grammatical revision of this paper.

References

1. Jayaram N, McNally B, Tang F, Chan PS. Survival After Out-of-Hospital Cardiac Arrest in Children. J Am Heart Assoc 2015;4:e002122.
2. Hara M, Hayashi K, Kitamura T. Outcomes differ by first documented rhythm after witnessed out-of-hospital cardiac arrest in children: an observational study with prospective nationwide population-based cohort database in Japan. Eur Heart J Qual Care Clin Outcomes

2017;3:83-92.

3. Khera R, CarlLee S, Blevins A, Schweizer M, Girotra S. Early coronary angiography and survival after out-of-hospital cardiac arrest: a systematic review and meta-analysis. Open Heart 2018;5:e000809.

4. Beyea MM, Tillmann BW, Iansavichene AE, Randhawa VK, Van Aarsen K, Nagpal AD. Neurologic outcomes after extracorporeal membrane oxygenation assisted CPR for resuscitation of out-of-hospital cardiac arrest patients: A systematic review. Resuscitation 2018;130:146-58.

5. Moler FW, Silverstein FS, Holubkov R, et al. Therapeutic Hypothermia after In-Hospital Cardiac Arrest in Children. N Engl J Med 2017;376:318-29.

6. Maconochie IK, de Caen AR, Aickin R, et al. Part 6: Pediatric basic life support and pediatric advanced life support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation 2015;95:e147-68.

7. Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med 2002;137:511-20.

8. Callaway CW, Schmicker R, Kampmeyer M, et al. Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. Resuscitation 2010;81:524-9.

9. Ro YS, Shin SD, Song KJ, et al. A comparison of outcomes of out-of-hospital cardiac arrest with non-cardiac etiology between emergency departments with low- and high-resuscitation case volume. Resuscitation 2012;83:855-61.

10. Shin SD, Suh GJ, Ahn KO, Song KJ. Cardiopulmonary resuscitation outcome of out-of-hospital cardiac arrest in low-volume versus high-volume emergency departments: An observational study and propensity score matching analysis. Resuscitation 2011;82:32-9.

11. 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.

12. Matsuyama T, Kiyohara K, Kitamura T, et al. Hospital characteristics and favourable neurological outcome among patients with out-of-hospital cardiac arrest in Osaka, Japan. Resuscitation 2017;110:146-53.

13. Carr BG, Kahn JM, Merchant RM, Kramer AA, Neumar RW. Inter-hospital variability in post-cardiac arrest mortality. Resuscitation 2009;80:30-4.

14. Tilford JM, Simpson PM, Green JW, Lensing S, Fiser DH. Volume-outcome relationships in pediatric intensive care units. Pediatrics 2000;106:289-94.

15. Marcin JP, Song J, Leigh JP. The impact of pediatric intensive care unit volume on mortality: a hierarchical instrumental variable analysis. Pediatric critical care medicine : a

journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 2005;6:136-41.

16. Markovitz BP, Kukuyeva I, Soto-Campos G, Khemani RG. PICU Volume and Outcome: A Severity-Adjusted Analysis. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 2016;17:483-9.

17. Amagasa S, Kashiura M, Moriya T, et al. Relationship between institutional case volume and one-month survival among cases of paediatric out-of-hospital cardiac arrest. Resuscitation 2019;137:161-7.

18. Iwagami M, Yasunaga H, Doi K, et al. Postoperative polymyxin B hemoperfusion and mortality in patients with abdominal septic shock: a propensity-matched analysis. Critical care medicine 2014;42:1187-93.

19. Sasaki R, Yasunaga H, Matsui H, Michihata N, Fushimi K. Hospital Volume and Mortality in Mechanically Ventilated Children: Analysis of a National Inpatient Database in Japan. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies 2016;17:1041-4.

20. Hsia RY, Dai M, Wei R, Sabbagh S, Mann NC. Geographic Discordance Between Patient Residence and Incident Location in Emergency Medical Services Responses. Ann Emerg Med 2017;69:44-51 e3.

21. Kiyohara K, Sado J, Kitamura T, et al. Epidemiology of Pediatric Out-of-Hospital Cardiac Arrest at School- An Investigation of a Nationwide Registry in Japan. Circ J 2018;82:1026-32.

22. Forrest A, Butt WW, Namachivayam SP. Outcomes of children admitted to intensive care after out-of-hospital cardiac arrest in Victoria, Australia. Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine 2017;19:150-8.

23. Scholefield BR, Gao F, Duncan HP, et al. Observational study of children admitted to United Kingdom and Republic of Ireland Paediatric Intensive Care Units after out-of-hospital cardiac arrest. Resuscitation 2015;97:122-8.

24. Gupta P, Tang X, Gall CM, Lauer C, Rice TB, Wetzel RC. Epidemiology and outcomes of in-hospital cardiac arrest in critically ill children across hospitals of varied center volume: a multi-center analysis. Resuscitation 2014;85:1473-9.

25. McCarthy JJ, Carr B, Sasson C, et al. Out-of-Hospital Cardiac Arrest Resuscitation Systems of Care: A Scientific Statement From the American Heart Association. Circulation 2018;137:e645-e60.

26. Heffner AC, Pearson DA, Nussbaum ML, Jones AE. Regionalization of post-cardiac arrest care: implementation of a cardiac resuscitation center. American heart journal 2012;164:493-501.e2.

27. Tranberg T, Lippert FK, Christensen EF, et al. Distance to invasive heart centre, performance of acute coronary angiography, and angioplasty and associated outcome in out-of-hospital cardiac arrest: a nationwide study. Eur Heart J 2017;38:1645-52.
28. McKenzie N, Williams TA, Ho KM, et al. Direct transport to a PCI-capable hospital is associated with improved survival after adult out-of-hospital cardiac arrest of medical aetiology. Resuscitation 2018;128:76-82.
29. Donoghue AJ, Nadkarni VM, Elliott M, Durbin D, American Heart Assocation National Registry of Cardiopulmonary Resuscitation I. Effect of hospital characteristics on outcomes from pediatric cardiopulmonary resuscitation: a report from the national registry of cardiopulmonary resuscitation. Pediatrics 2006;118:995-1001.
30. Michelson KA, Hudgins JD, Monuteaux MC, Bachur RG, Finkelstein JA. Cardiac Arrest Survival in Pediatric and General Emergency Departments. Pediatrics 2018;141.
31. Yamana H, Moriwaki M, Horiguchi H, Kodan M, Fushimi K, Yasunaga H. Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. Journal of epidemiology 2017;27:476-82.
32. 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.

Figure Legends

Figure 1. Flowchart of patient inclusion

Figure 2. Incidence of primary and secondary outcomes (%)

[a] Hospital category was defined as the mean annual number of paediatric cases involving invasive mechanical ventilation; low (<=48); low-intermediate (>48, <=101); high-intermediate (>101, <=164); and high (>164).

Table1

Table 1. Participants' baseline characteristics according to hospital category defined by the average number of paediatric invasive mechanical ventilation cases

Hospital category (annual number of paediatric patients with invasive mechanical ventilation)	Low (<48)	Low-intermediate (48–101)	High-intermediate (101–164)	High (>164)	p value
Institutions					
Number of institutions (%)	206 (100)	80 (100)	58 (100)	41 (100)	
Academic (%)	11 (5.3)	21 (26.3)	29 (50.0)	13 (31.7)	<.001
Emergency care centre (%)	85 (41.3)	52 (65.0)	33 (56.9)	24 (58.5)	.004
Patients					
Basic characteristics					
Number of patients (%)	624 (100)	626 (100)	651 (100)	639 (100)	
Men (%)	375 (60.1)	376 (60.1)	377 (57.9)	404 (63.2)	.410
Age (years, median [IQR])	8.4 [0.7–15.4]	5.1 [0.8–14.0]	4.2 [0.6–13.4]	2.7 [0.5–11.8]	<.001
Distance (km, median [IQR])	5.1 [2.7–10.5]	5.7 [2.9–11.7]	6.2 [3.3–15.8]	7.2 [4.2–15.2]	<.001
Comorbid diagnosis					
Ventricular fibrillation (%)	85 (13.6)	119 (19.0)	129 (19.8)	84 (13.1)	.900
Trauma (%)	42 (6.7)	28 (4.5)	32 (4.9)	24 (3.8)	.030
CHD (%)	22 (3.5)	19 (3.0)	25 (3.8)	39 (6.1)	.020
Congenital disease other than CHD (%)	22 (3.5)	26 (4.2)	23 (3.5)	42 (6.6)	.020
Treatment					
Mechanical ventilation (%)	539 (86.4)	516 (82.4)	532 (81.7)	559 (87.5)	.680
Catecholamine infusion (%)	554 (88.8)	551 (88.0)	584 (89.7)	550 (86.1)	.260
TTM (%)	102 (16.3)	82 (13.1)	91 (14.0)	122 (19.1)	.160
ECMO (%)	30 (4.8)	20 (3.2)	25 (3.8)	19 (3.0)	.150
CHDF (%)	14 (2.2)	25 (4.0)	17 (2.6)	18 (2.8)	.920

CHD = congenital heart disease; CHDF = continuous hemodiafiltration; ECMO = extracorporeal membrane oxygenation; IQR = inter quartile range; TTM = targeted temperature management.

Table2

Table 2. Results of univariable and multivariable logistic regression analyses for the primary outcome (in-hospital mortality)

	Univariable			Multivariable		
	OR	[95%CI]	p value	OR	[95%CI]	p value
Hospital category						
low	reference			reference		
low-intermediate	0.94	[0.78-1.37]	0.54	0.63	[0.40-1.01]	0.053
high-intermediate	0.97	[0.80-1.16]	0.84	0.67	[0.42-1.05]	0.080
high	0.74	[0.62-0.89]	0.001	0.46	[0.31-0.70]	<0.001
Other hospital characteristics						
emergency center	1.57	[1.32-1.87]	<0.001	1.28	[0.92-1.76]	0.140
academic	0.56	[0.47-0.66]	<0.001	0.96	[0.67-1.38]	0.835
Patient background						
age (year)	0.91	[0.9-0.92]	<0.001	1.00	[1.00-1.00]	0.001
men	0.90	[0.77-1.07]	0.228	1.02	[0.81-1.28]	0.891
distance (km)	1.00	[0.99-1.00]	<0.001	1.00	[1.00-1.00]	0.001
year	1.03	[0.98-1.07]	0.22	1.04	[0.97-1.11]	0.283
Comorbid diagnosis on admission						
congenital heart disease	0.86	[0.58-1.29]	0.48	0.58	[0.35-0.98]	0.042
congenital disease other than CHD	0.78	[0.53-1.14]	0.2025	0.52	[0.32-0.85]	0.009
Vf/VT	0.03	[0.02-0.04]	<0.001	0.04	[0.02-0.06]	<0.001
Trauma	2.41	[1.55-3.74]	<0.001	1.37	[0.80-2.35]	0.259
Treatment						
catecholamine infusion	7.66	[5.74-10.20]	<0.001	14.83	[10.59-20.80]	<0.001
mechanical ventilation	8.00	[6.21-10.30]	<0.001	2.79	[1.84-4.23]	<0.001
TTM	0.22	[0.18-0.28]	<0.001	0.10	[0.08-0.13]	<0.001
ECMO	1.37	[0.88-2.14]	0.16	3.04	[1.25-7.35]	0.014
CHDF	0.83	[0.52-1.33]	0.45	0.75	[0.32-1.73]	0.495

OR = odds ratio of mortality; CI = confidence interval; CHD = congenital heart disease; TTM = targeted temperature management; ECMO = extracorporeal membrane oxygenation; CHDF = continuous hemodiafiltration.

Table3

Table 3. Results of multivariable logistic regression analyses for the secondary outcome (death or medical care dependency at discharge)

	Multivariable						
	OR	[95%CI]					p value
Hospital category							
low	reference						
low-intermediate	0.93	[	0.55	-	1.57	]	0.789
high-intermediate	0.95	[	0.63	-	1.43	]	0.795
high	0.67	[	0.46	-	0.96	]	0.030
Other hospital characteristics							
emergency center	1.20	[	0.89	-	1.63	]	0.240
academic	0.80	[	0.56	-	1.15	]	0.231
Patient background							
age (year)	1.00	[	1.00	-	1.00	]	<.001
men	0.83	[	0.83	-	1.35	]	0.661
distance(km)	1.00	[	1.00	-	1.00	]	<.001
year	0.97	[	0.91	-	1.03	]	0.303
Comorbid diagnosis on admission							
congenital heart disease	0.77	[	0.43	-	1.40	]	0.389
congenital disease other than CHD	0.65	[	0.40	-	0.06	]	0.084
Vf/VT	0.04	[	0.03	-	0.07	]	<.001
Trauma	1.04	[	0.59	-	1.83	]	0.905
Treatment							
catecholamine infusion	8.95	[	6.34	-	12.6	]	<.001
mechanical ventilation	4.41	[	3.03	-	6.41	]	<.001
TTM	0.11	[	0.08	-	0.14	]	<.001
ECMO	2.25	[	0.96	-	5.24	]	0.061
CHDF	0.70	[	0.32	-	1.55	]	0.374

OR = odds ratio; CI = confidence interval; CHD = congenital heart disease; TTM = targeted temperature management; ECMO = extracorporeal membrane oxygenation; CHDF = continuous hemodiafiltration.

Table4

Table 4. Results of multivariable logistic regression analyses for in-hospital mortality, stratified by age group

Hospital category	Low	Low-intermediate	High-intermediate	High
Infant (age <1 year)				
aOR[a]	reference	0.82	1.01	0.44
[95%CI]	-	[0.37-1.87]	[0.46-2.23]	[0.22-0.9]
p value	-	0.639	0.976	0.024
Toddler (age >=1, <6)				
aOR[a]	reference	0.33	0.35	0.33
[95%CI]	-	[0.14-0.76]	[0.15-0.82]	[0.15-0.76]
p value	-	0.009	0.016	0.009
School age (age>=6, <18)				
aOR[a]	reference	0.75	0.64	0.53
[95%CI]	-	[0.43-1.3]	[0.35-1.16]	[0.32-0.88]
p value	-	0.3	0.14	0.014

aOR = adjusted odds ratio; CI = confidence interval.

[a] Independent variables include academic, board-certified emergency care center, age, sex, year of hospitalization, transport distance, ventricular fibrillation, trauma, congenital heart disease, congenital disease other than congenital heart disease, mechanical ventilation, catecholamine infusion, targeted temperature management, extracorporeal membrane oxygenation and continuous hemodiafiltration.

Figure 1

Figure 1. Flowchart of patient inclusion

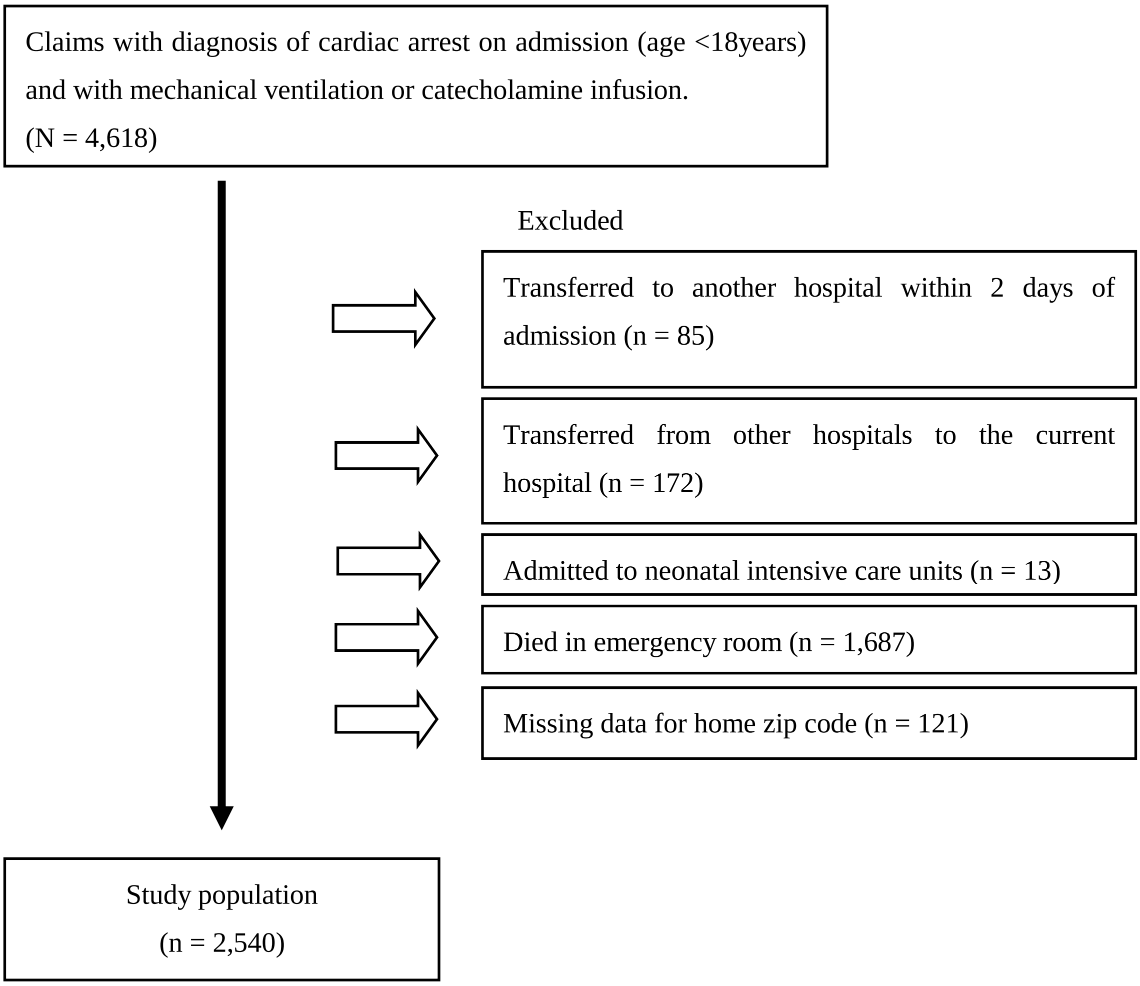
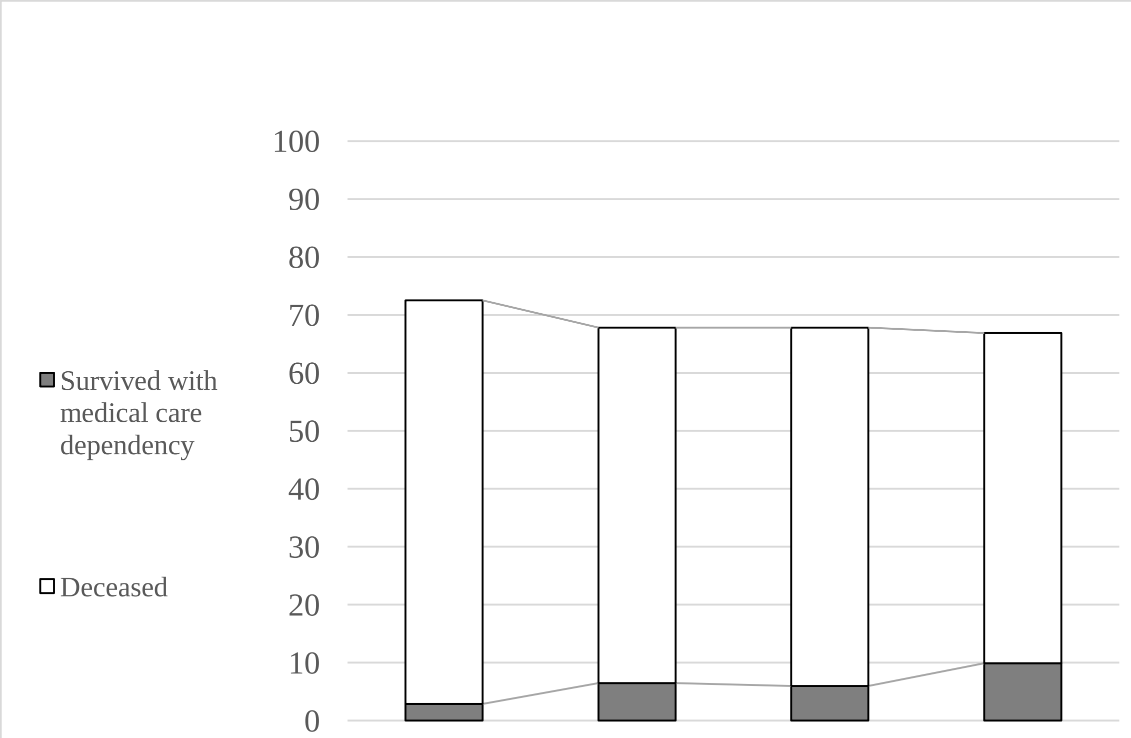


Figure 2

Figure 2. Incidence of primary and secondary outcomes (%)



Hospital category[a]	**Low (N = 624)**	**Low-intermediate (N = 626)**	**High-intermediate (N = 651)**	**High (N = 639)**
Deceased, n (%)	434 (69.6)	384 (61.3)	402 (61.8)	364 (57.0)
Deceased or medical care dependent, n (%)	452 (72.4)	425 (67.9)	441 (67.7)	421 (65.9)