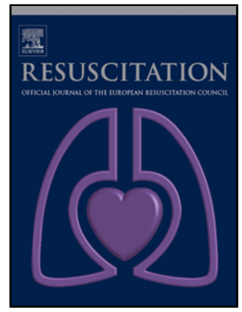

Title: Epidemiology and outcome of paediatric out-of-hospital cardiac arrests: A paediatric sub-study of the Pan-Asian resuscitation outcomes study (PAROS)

Authors: Lai Peng Tham, Win Wah, Rachel Phillips, Nur Shahidah, Yih Yng Ng, Sang Do Shin, Tatsuya Nishiuchi, Kwanhathai Darin Wong, Patrick Chow-In Ko, Nalinas Khunklai, Ghulam Yasin Naroo, Marcus Eng Hock Ong

PII: S0300-9572(18)30049-2
DOI: https://doi.org/10.1016/j.resuscitation.2018.01.040
Reference: RESUS 7471

To appear in: *Resuscitation*

Received date: 6-8-2017
Revised date: 27-12-2017
Accepted date: 26-1-2018

EPIDEMIOLOGY AND OUTCOME OF PAEDIATRIC OUT-OF-HOSPITAL CARDIAC ARRESTS: A PAEDIATRIC SUB-STUDY OF THE PAN-ASIAN RESUSCITATION OUTCOMES STUDY (PAROS)

1. Lai Peng Tham

   Department of Emergency Medicine, KK Women's and Children's Hospital, Singapore, Singapore

2. Win Wah

   Department of Emergency Medicine, Singapore General Hospital, Singapore

3. Rachel Phillips

   Department of Primary Care and Public Health Sciences, King's College London, London, United Kingdom

4. Nur Shahidah

   Department of Emergency Medicine, Singapore General Hospital, Singapore, Singapore

5. Yih Yng Ng

   Medical Department, Singapore Civil Defence Force, Singapore, Singapore

6. Sang Do Shin

   Department of Emergency Medicine, College of Medicine, Seoul National University, Seoul, Korea

7. Tatsuya Nishiuchi

   Department of Acute Medicine, Kindai University Faculty of Medicine, Osaka, Japan

8. Kwanhathai Darin Wong

   Emergency Department, Hospital Pulau Pinang, Penang, Malaysia

9. Patrick Chow-In Ko

   Department of Emergency Medicine, National Taiwan University Hospital, National Taiwan University, Taipei, Taiwan

10. Nalinas Khunklai

Department of Emergency Medicine, Rajavithi Hospital, Bangkok, Thailand

11. Ghulam Yasin Naroo

Department of Health and Medical Services, ED-Trauma Center, Rashid Hospital, Dubai, United Arab Emirates

12. Marcus Eng Hock Ong, for the PAROS Clinical Research network

Department of Emergency Medicine, Singapore General Hospital, Singapore, Singapore Health Services and Systems Research, Duke-NUS Graduate Medical School, Singapore, Singapore, for the PAROS Clinical Research Network

Corresponding Author:
Dr. Lai Peng Tham
Department of Emergency Medicine
KK Women's and Children's Hospital
Singapore 229899
Email: tham.lai.peng@singhealth.com.sg

ABSTRACT

Background

The Pan Asian Resuscitation Outcomes Study (PAROS) is a retrospective study of out- of-hospital cardiac arrest(OHCA), collaborating with EMS agencies and academic centers in Japan, South Korea, Malaysia, Singapore, Taiwan, Thailand and UAE-Dubai. The objectives of this study is to describe the characteristics and outcomes, and to find factors associated with survival after paediatric OHCA.

Methods

We studied all children less than 17 years of age with OHCA conveyed by EMS and non-EMS transports from January 2009 to December 2012. We did univariate and multivariate logistic regression analyses to assess the factors associated with survival-to-discharge outcomes.

Results

A total of 974 children with OHCA were included. Bystander cardiopulmonary resuscitation rates ranged from 53.5% (Korea), 35.6% (Singapore) to 11.8%(UAE). Overall, 8.6% (range 0% to 9.7%) of the children survived to discharge from hospital. Adolescents (13-17 years) had the highest survival rate of 13.8%. 3.7% of the children survived with good neurological outcomes of CPC 1 or 2. The independent pre-hospital factors associated with survival to discharge were witnessed arrest and initial shockable rhythm. In the sub-group analysis, pre-hospital advanced airway [odds ratio (OR) =3.35, 95% confidence interval (CI) =1.23 - 9.13] was positively associated with survival-to-discharge outcomes in children less than 13 years-old. Among adolescents, bystander CPR (OR=2.74, 95%CI=1.03-7.3) and initial shockable rhythm (OR=20.51, 95%CI = 2.15-195.7) were positive factors.

Conclusion

The wide variation in the survival outcomes amongst the seven countries in our study may be due to the differences in the delivery of pre-hospital interventions and bystander CPR rates.

Keywords: Paediatric; pediatric; out-of-hospital cardiac arrest; resuscitation; pre-hospital; Emergency Medical Service; epidemiology; outcome; Pan Asian Resuscitation Outcome Study

INTRODUCTION

Paediatric out-of-hospital cardiac arrests (OHCA) are uncommon when compared to adults. Survival following paediatric OHCA is less than 10% and associated with poor neurological outcomes.[1-5] However, wide variations in survival outcomes can exist between communities, and it has been suggested that these differences are mainly due to differences in how pre-hospital emergency care is delivered. [6-7] The Emergency Medical Services systems in the Asia-pacific region are diverse in terms of service level (predominantly Basic Life Support, BLS or Advanced Life Support, ALS) and resources (ambulances/ protocols/ medical oversight).[8] Except for reports from specific countries, little is known about the epidemiology and outcome of paediatric OHCA in the Asia-pacific region. [9-11]

The Pan Asian Resuscitation Outcomes Study (PAROS) Clinical Research Network, established in 2010,[12,13] is an international, multicenter, prospective registry of OHCA across the Asia-Pacific region, collaborating with the EMS agencies and academic centers in seven countries (Japan, South Korea, Malaysia, Singapore, Taiwan, Thailand and UAE-Dubai).

The objectives of this study are to give an overview of the state of paediatric resuscitation across seven countries in Asia, to describe the characteristics and outcomes of paediatric OHCA and to find factors associated with survival for paediatric OHCA within the Asia –pacific region.

METHODS

Study design and setting

This study was a retrospective analysis of PAROS study data from January 2009 to December 2012. PAROS study is a prospective, observational, multi-center cohort study in the participating PAROS sites (12 sites from seven countries). The 12 sites were: Japan (Tokyo, Aichi, Osaka), Korea (Seoul), Malaysia (Klang Valley, Kota Bahru, Penang), Singapore, Taiwan (Taipei), Thailand (Bangkok, Songkhla) and UAE (Dubai). Each site contributed 1 to 3 years of data during the study period.

The ambulance-to-population ratio among the participating sites ranged from 1:14,000 to 1:218,000 with the population density ranging from 474.8 per km2 to 19014.4 per km2.[8] The socioeconomic status and the EMS systems in the PAROS participating sites/ countries are diverse, and have been described in previous publications.[8] The EMS systems in Japan, Korea and Singapore were mainly single tiered (Basic Cardiac Life Support with Automatic External Defibrillator, AED certified), fire-based and the ambulance personnel were mostly emergency medical technicians (EMT-intermediate level). For Thailand and Malaysia, the EMS systems were hospital-based, and in Thailand, the personnel included nurses and physicians that may be ALS trained). The EMS also differed in the dispatch systems, response times, airway management capabilities and drugs administered.[12]

Waiver of consent was approved by the local Institutional Review Boards in the participating countries as only clinical documents were reviewed for all the enrolled cardiac arrest cases. There was no patient or family interaction or intervention involved. All patient identifiers were removed from the dataset to protect patients' privacy and confidentiality.

<u>Participants</u>

All children and adolescents less than 17 years of age conveyed by EMS, or presenting to Emergency Departments (ED) in cardiac arrest during the study period, as confirmed by the absence of pulse, unresponsiveness and apnoea were included. For Malaysia, Singapore and Thailand, OHCA patients who were conveyed to the EDs by non-EMS private transports were also included, as a significant portion of the collapsed children were brought in by their care-givers in their own transports. We excluded cases that were immediately pronounced dead, and resuscitation was not attempted, including decapitation, rigor mortis and dependent lividity. However, patients were included when resuscitation was attempted but were subsequently pronounced dead at field (Malaysia and Thailand).

Data collection and management

A data collection/ case record form with standardized taxonomy was used by all the participating countries to collect the common variables. The variables were categorized into core and non-core (optional). The data was extracted from emergency dispatch records, ambulance patient case notes, emergency department and in-hospital records and entered into a secured shared internet electronic data capture (EDC) network. This was then sent to the Study Co-ordination Center in Singapore (hosting country) for data management. Countries with existing national registries (Japan, South Korea and Taiwan) contributed data via an export field entry process, which auto-populated the PAROS registry. Variables which were not captured in these countries' original databases were determined and then converted to the EDC format according to the reconciliation rules. The datasets from all the participating sites were merged and analyzed.[12] The data was collected between the period of January 2009 to December 2012 with each country contributing between 1 to 3 years of data.

Study Variables

The epidemiological data studied were: demographics (age, gender, race, and country), pre-hospital data (transported by EMS or private vehicle, location where the cardiac arrest occurred, any past medical history, witnessed arrest - EMS paramedics or bystander, bystander CPR rates - compression only or both ventilation and compressions, first CPR initiated by whom, first arrest rhythm, pre-hospital defibrillation and performed by bystander or EMS, mechanical CPR and which type, pre-hospital advanced airway and which type – endotracheal tube/ET, laryngeal mask airways/LMA, others, pre-hospital drug administration - adrenaline, atropine, amiodarone and dextrose, pre-hospital return of spontaneous circulation, final status at scene – conveyed to ED or pronounced dead at scene and time intervals – arrest to call, call to arrival at scene/ response time, arrival at scene to leave scene/ scene time, leave location to arrival at hospital/ en-route time), ED data (cardiac rhythm, defibrillation, mechanical CPR, advanced airway -ET, LMA, medications administered, hypothermia therapy, Extracorporeal membrane oxygenation/ECMO, etiology – trauma, cardiac, respiratory, drowning, electrocution or others).

The primary outcome studied was survival to hospital discharge. The secondary outcomes were return of spontaneous circulation (at scene or ED) defined as regaining of palpable pulse (sustained or transient) and survival with good neurological status (Cerebral Performance Categories 1 and 2). The neurological status is measured either at discharge, or at 30th day post arrest if not discharged.

The factors associated with the primary outcome (survival-to-discharge) identified a priori and analyzed were: age (categorized 0-1 year old, 1-5 years old, 6-12 years old, 13-17 years old), witnessed arrest, bystander CPR, pre-hospital advanced airway, pre-hospital defibrillation, pre-hospital drug administration, EMS time intervals (response time and scene time), initial cardiac rhythm and etiology of cardiac arrest.

Statistical analysis

The demographic and clinical characteristics of paediatric OHCA were compared among PAROS countries. We did univariate and multivariate logistic regression analyses to assess the factors associated with survival-to-discharge outcomes. Association with survival-to-discharge outcomes was assessed after adjusting for prehospital demographic and clinical characteristics. We selected the predictor variables based on whether they were reported in the literature[1-5] or they were significant in the univariate analysis ($p<0.1$) and used the backward-stepwise procedures in the multivariate models. The model selection was done using the Akaike's

Information Criterion (AIC) and Bayesian information criterion (BIC). We performed sub-group analyses stratified by age group (<13, ≥13). The cut-off age of less than or more than 13 years was used because the univariate analysis showed that older children 13 years or more had the best prognosis and the hypothesis is that they may have a different set of prognosticating factors compared with younger children. Categorical characteristics were compared using chi-squared test or Fisher exact test. Independent samples t-test was used to compare normally distributed continuous variables and Mann-Whitney U test was used to compare the continuous variables (time between call and ambulance arriving at scene, time between ambulance arriving at scene and leaving scene) which were not normally distributed. Statistical significance was set at $p<0.05$. All data analyses were performed with Stata version 14 (StataCorp, College Station, TX, USA).

RESULTS

Demographics of paediatric OHCA

A total of 974 children and adolescents less than 17 years with OHCA were included in the study. This constituted 1.5% of the total number of patients (N=66780) in the PAROS database. Fig. 1 describes the overall patient flowchart. The numbers of patients enrolled in each of the participating PAROS countries is shown in Table 1. The median age of the patients was 2 (Interquartile range/IQR=0-12) years, with 60.6% male.

Characteristics of paediatric OHCA

The majority (67.6%) of the cardiac arrests occurred in the home residence (Table 1). 60.1% of the OHCA events were unwitnessed, with 31.7% witnessed by bystanders (laypersons, healthcare providers or family members) and 5.5% by EMS personnel. Overall 49.2% of the children received bystander CPR, ranging from 53.5% in Korea to 35.6% in Singapore and 11.8% in UAE (Table 2).

Only 46 (4.8%) children presented with ventricular fibrillation (VF)/ ventricular tachycardia (VT) or an unknown shockable rhythm. 6.5% of the children received defibrillation at the prehospital setting, delivered either by bystanders or ambulance crew. 22 of these children who received defibrillation had a non-shockable rhythm. 5.7% of the patients arrived in ED with persistent shockable rhythm and received defibrillation.

127 (13%) children received advanced airway management by the ambulance crew, of which 18 (1.8%) had endotracheal intubations, 79 (8.1%) had supraglottic airways and 29 (3%) had other types of advanced airway. Only 19 (2%) of the children were administered epinephrine.

25.3% of the children sustained cardiac arrest due to trauma. The remaining 74.7% of the children had presumed cardiac etiology, respiratory, electrocution, drowning or other causes.

<u>EMS timings</u>

Table 3 shows the EMS timings for the PAROS participating sites. The mean EMS response time (time of call to time ambulance arrived at scene) varied from 6.3min (SD 3.6 min) in Japan to 20.6 min (SD 8.5 min) in Malaysia. The scene time varied from a mean of 5.5 min (SD 4.4 min) in Korea to 19.1 min (SD 21.1 min) in Malaysia.

<u>Outcomes of paediatric OHCA</u>

7.4% of the patients had ROSC before arrival to hospital. Overall, 84 (8.6%) of the children survived to discharge from hospital, with range of 0% to 9.7% among the seven countries (Table 3). Infants had the lowest survival rate of 6.1%, followed by young children (1-5 years old) at 9.8%, older children (6 – 12 years old) at 7.5% and highest in adolescents (13 – 17 years old) at 13.8%. 3.7% of the children survived with good neurological outcome of CPC 1 or 2. The mean response time among those who survived was 6.3 min versus 6.4min in those who died. Mean scene time was 10.5 min for the survivors versus 8.5min in the non-survivors.

Table 4 shows the pre-hospital factors associated with survival to discharge using a logistic regression model. In the multivariate analysis, only witnessed arrest and initial shockable rhythms show independent association with improved survival-to-discharge outcomes. In the sub-group analysis, after adjusting for pre-hospital characteristics (Table 5), arrest witnessed by EMS and bystanders and pre-hospital advanced airway show an independent, positive association with survival-to-discharge outcomes in children less than 13 years. In adolescents age 13 years and above, arrest witnessed by bystanders, bystander CPR and initial shockable rhythms were independently associated with better survival-to-discharge outcomes.

DISCUSSION

This is the first multi-center study involving seven countries in the Asia-pacific region, reporting the epidemiology and outcomes of paediatric out-of-hospital cardiac arrests using a standardized data collection template, though there is previous published data from a few individual countries in Asia-pacific region.[3,9,10,11] Paediatric patients less than 17 years old constitutes only 1.5% of the total number of PAROS enrolled patients. This small number is similar to other OHCA registries, such as the CARES registry[14] that reported 2.2% children less than 18 years, reflecting the low prevalence of OHCA in this age group.

The overall survival to discharge rate was 8.6% in our paediatric study, ranging from 0 – 9.7%. This is higher than the overall survival rate of 5.4% (range 0.5 – 8.5%) reported in the main PAROS paper which included all age groups,[12] and the survival rate of 7.8% for young adults aged 16 to 35 years reported from the same PAROS database.[16] Also, more children survived with good neurological outcome (post arrest CPC 1 or 2) as compared to all age groups (3.7% vs 2.7%) in the main PAROS study.[12] This trend was observed in other reported studies, and the survival rates within each paediatric age category were also similar.[1,9-10,14-15]

Within the paediatric age categories, adolescents aged 13 to 17 years had the most favorable outcome when compared to children aged less than 13 years old. It is likely that adolescents had more favorable arrest characteristics such as witnessed arrest and initial shockable rhythm as these two factors were shown to be independently associated with higher odds of survival to discharge outcomes in the multivariate analysis. Bystander CPR was also a factor associated with better survival to discharge outcome in the adolescents, though not in the younger age group. The bystander CPR rates varied between 4.2% in Thailand to 53.5% in Korea and this may explain the poorer outcomes in countries which also had low bystander CPR rates. The high bystander CPR rates in Japan were due to comprehensive efforts on community CPR education over the recent decades, with involvement of schools and fire department and driver license CPR programmes. In Korea (Seoul), nurse telephone assisted CPR increased bystander performance rates before arrival of ambulance crew.

The use of AEDs has been shown to be less prevalent in the younger paediatric age groups (1 – 8 years) when compared with older children (9-17 years) and adults in a study conducted in the US (16.3%, 20.5% and 28.3%).[14] This was attributed to the lower prevalence of initial shockable rhythm in young children (11.6%) compared with adults (23.7%). This contrasts with our study which reported an even lower prevalence rate of initial shockable rhythm (VT/VF/unknown shockable rhythm) (4.8%) and pre-hospital defibrillation rate (6.5%). The low initial shockable rhythm rate in our study may be related to the infrequent use of AEDs in the prehospital setting and it is possible that some of the shockable rhythms may have been missed. However, this may also represent a true racial difference in the prevalence of shockable rhythms in paediatric cardiac arrest between the Asian and United States populations. As initial shockable rhythm is a factor associated with survival, ensuring that EMS ambulances are equipped with paediatric AED pads and that personnel are trained in AED use when responding to all paediatric cardiac arrest, will help to improve outcome.[22-24]

In our study, advanced airway management was performed in all the participating countries except Malaysia, although the rate was low at only 13%, compared with other published studies of 14.3% to 73%.[1, 15, 25] However, in our study, advanced airway management was found to be positively associated with favorable outcome in the younger children less than 13 years old. The reason could be that most cardiac arrests in the younger children were due to respiratory causes and advanced airway may contribute to more effective ventilation especially en-route to hospital with ongoing CPR.

Resuscitative drugs were only administered in 2% of the children in our study as compared to 30% in the ROC study.[1] Resuscitative drugs (epinephrine, atropine, amiodarone, dextrose) were not found to be associated with survival to hospital discharge in our study. This is similar with findings from other studies, [1, 25, 26] but in at least two studies,[15, 27] administering of epinephrine was associated with increased mortality. These studies suggested that resuscitative drugs in the pre-hospital settings may not increase survival rates in children, but further larger prospective studies are needed regarding the role of epinephrine and other resuscitation drugs.

Among the sites/ countries involved in this study, Korea and Japan had the most favorable outcomes, though their EMS systems are EMT-intermediate systems, as compared with ALS in Dubai and tiered-response systems (BLS and ALS) in Taiwan and Bangkok. Better training in the basic and intermediate skills that the rescuers have in Korea and Japan, such as high-quality CPR, higher successful advanced airway intervention (supra-glottic airways) rates and routine use of AED defibrillation for all paediatric cardiac arrests, together with higher bystander CPR rates may have contributed to better outcomes.

Limitations

We were unable to report the incidence of paediatric OHCA in each country or state (province) due to incomplete population based data for majority of the sites involved. Also, in the countries that the EMS systems are still developing, a fairly significant proportion of the patients, especially in the paediatric population, may have been brought to the hospitals by private or public transport and these patients' data and outcome may not have been captured in the database in some of the participating sites.[12] The number of enrolled children in some of the participating sites were very small, likely to be due to incomplete enrollment. Considering that most of the patients enrolled were contributed by Japan, the overall results and data may need to be interpreted accordingly.[12]

Additionally, OHCA survival reported in countries (Malaysia and Thailand) that allowed ambulance personnel to terminate resuscitation in the field when futile, under direct physician orders, might not be fully representative of those populations. Therefore, the results of this study might not be completely generalized to all included sites. Moreover, differences in patients, EMS and hospital characteristics might influence the comparability of outcomes across countries. However, this multi-center study managed these bias by using standardized case definitions and data collection methods across participating sites.

There was small amount of missing data on the primary outcomes of survival -to-discharge (3.1%), and CPC (2.3%). We did several sensitivity analyses on the eligible cohort and subgroups by considering missing survival-to-discharge outcomes as non-survivors and by excluding missing survival-to-discharge outcomes. We observed similar results in the sensitivity analyses.

In view of the relatively small number of survivals, this study is not powered to determine pre-hospital interventions that result in favorable or good neurological outcomes.

CONCLUSION

This first multi-center study involving seven countries in the Asia-pacific region showed that wide variation in the survival rates amongst the seven countries in our study may be due to the differences in the EMS systems in terms of quality of CPR, bystander CPR rate and pre-hospital interventions. This study also highlighted that bystander CPR was a significant predictor for better survival-to-discharge outcomes among adolescents aged 13 to 17 years. Therefore, further training to improve EMS performance and future research on implementation of CPR feedback devices in ambulances, and dispatcher assisted CPR across the participating sites may improve the outcome in paediatric OHCA across the countries.

Conflict of interest: none
PAROS Clinical Research Network
Participating Site Investigators: NAR Hisamuddin (School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia), MN Julina (Hospital Sungai Buloh, Selangor, Malaysia), AS Omer (Dubai Corporation for Ambulance Services, Dubai, United Arab Emirates), T Yagdir (Dubai Corporation for Ambulance Services, Dubai, United Arab Emirates), P Khruekarnchana (Rajavithi Hospital, Bangkok, Thailand), A Monsomboon (Siriraj Hospital, Bangkok, Thailand), T Piyasuwankul (Prince of Songkla University, Hatyai, Thailand), KD Wong (Hospital Pulau Pinang, Pulau Pinang, Malaysia), ES Goh (Khoo Teck Puat Hospital, Singapore), NE Doctor (Singapore General Hospital, Singapore), LP Tham (KK Women's & Children's Hospital, Singapore), K Kajino (Osaka National Hospital, Osaka, Japan), RA Charles (Alexandra Hospital, Singapore), DCG Foo (Tan Tock Seng Hospital, Singapore), HN Gan (Changi General Hospital, Singapore), MHM Ma (Department of Emergency Medicine, National Taiwan University, Taipei, Taiwan), SD Shin (Department of Emergency Medicine, College of Medicine, Seoul National University, Seoul, Republic of Korea).

Funding source:

This study is supported by grants from the National Medical Research Council (Singapore) and Ministry of Health, Singapore, and Korea Centers for Disease Control and Prevention..

Acknowledgements

We would like to acknowledge the contributions of Ms. Pek Pin Pin and Susan Yap from the Department of Emergency Medicine, Singapore General Hospital for coordination of the study.

REFERENCES

1. Atkins DL, Everson-Stewart S, Sears GK, et al, on behalf of the ROC Investigators. Epidemiology and outcomes from out-of-hospital cardiac arrest in children: the resuscitation outcomes consortium epistry-cardiac arrest. Circulation 2009;119:1484–91.2.
2. Young KD, Gausche-Hill M, McClung CD, Lewis RJ. A prospective, population-based study of the epidemiology and outcome of out-of-hospital pediatric cardiopulmonary arrest. Pediatrics 2004; 114:157–64.4.
3. Deasy C, Bernard SA, Cameron P, et al. Epidemiology of paediatric out-of-hospital cardiac arrest in Melbourne, Australia. Resuscitation 2010; 81:1095–100.7.
4. Donoghue AJ, Nadkarni V, Berg RA, et al., CanAm Pediatric Cardiac Arrest Investigators. Out-of-hospital pediatric cardiac arrest: an epidemiologic review and assessment of current knowledge. Ann Emerg Med 2005;46:512–22.8.
5. Herlitz J, Svensson L, Engdahl J, et al. Characteristics of cardiac arrest and resuscitation by age group: an analysis from the Swedish Cardiac Arrest Registry. AmJ Emerg Med 2007;25:1025–31.9.
6. McNally B, Robb R, Mehta M, et al. Out-of-hospital cardiac arrest surveillance – Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1,2005 – December 31, 2010. MMWR CDC Surveill Summ 2011;60:1–1
7. Okamoto Y, Iwami T, Kitamura T, et al. Regional variation in survival following pediatric out-of-hospital cardiac arrest. Circ J 2013; 77: 2596 – 2603
8. Shin SD, Ong MEH, Tanaka H, et al. Comparison of Emergency Medical Services Systems across Pan-Asian Countries: a Web-based Survey. Prehospital Emergency Care 2012; 16:477-96.
9. Park CB, Shin SD, Suh GJ, et al. Pediatric out-of-hospital cardiac arrest in Korea: A nationwide population-based study. Resuscitation 2010;81:512–7.
10. Nitta M, Iwami T, Kitamura T et al. Age-specific differences after out-of-hospital cardiac arrests. Pediatr 2011;128: e812-20.
11. Tham LP, Chan I. Paediatric out-of-hospital cardiac arrests: epidemiology and outcome. Singapore Med J 2005;46: 289-96.
12. Ong MEH, Shin SD, De Souza NNA, et al. Outcomes for out-of-hospital cardiac arrests across 7 countries in Asia: The Pan-Asian Resuscitation Outcomes Study (PAROS). Resuscitation 2015; 96:100 – 8.
13. Ong MEH, Shin SD, Tanaka H et al. Pan Pan-Asian Resuscitation Outcomes Study (PAROS): Rationale, Methodology, and Implementation. Acad Emerg Med 2011; 18:890–7.
14. Johnson MA, Grahan BJH, Haukoos JS, et. al. Demographics, bystander CPR, and AED use in out-of-hospital pediatric arrests. Resuscitation 2014;85: 920-6.
15. Tijssen JA, Prince DK, Morrison DL 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.

16. Chia MY, Lu QS, NH Rahman, et al. PAROS Research network. Characteristics and outcomes of young adults who suffered an out-of-hospital cardiac arrest (OHCA). Resuscitation 2017; 111:34-40. doi: 10.1016
17. 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.
18. Akahane M, Tanabe S, Ogawa T et. al. Characteristics and outcomes of pediatric out-of-hospital cardiac arrest by scholastic age category. Pediatr Crit Care med 2013; 14: 130-6.
19. 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 doi: 10.1161.
20. Akahane M, Ogawa T, Tanabe S eta l. Impact of telephone dispatcher assistance on the outcomes of pediatric out-of-hospital cardiac arrest. Crit Care Med 2012; 40:1410-6.
21. Kitamura T, Iwami T, Kawamura T, et al. Conventional and chest compression- only cardiopulmonary resuscitation by bystanders for children who have out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. Lancet. 2010; 375:1347–54.
22. Topjian A, Berg RA. Pediatric Out-of-Hospital Cardiac Arrest. Circulation 2012; 125:2374-8.
23. Rossano JW, Jones WE, Lerakis S, et al. The Use of Automated External Defibrillators in infants. A report from the American Red Cross scientific advisory council. Pediatr Emerg Care 2015; 31: 526 – 30.
24. Fraser KN, Kou MM, Howell JM, Fullerton KT, Sturek C. Improper defibrillator pad usage by emergency care providers for children: an opportunity for re-education. American J Emerg Med 2014; 32:953-7.
25. Abe T, Nagata T, Hasegawa M, Hagihara A. Life support techniques related to survival after out-of-hospital cardiac arrest in infants. Resuscitation 2012: 612-8.
26. Gausche M, Lewis RJ, Stratton SJ et al. Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome: a controlled clinical trial. JAMA 2000; 283: 783-90.
27. Moler FW, Donaldson AE, Meert k et al. Multicenter cohort study of out-of-hospital pediatric cardiac arrest. Crit Care Med 2011; 39: 141 -9.

FIGURE LEGEND:

Figure 1: Flow chart of included paediatric out-of-hospital cardiac arrests

Figure 1: Flow diagram of all patients with out-of-hospital cardiac arrest.

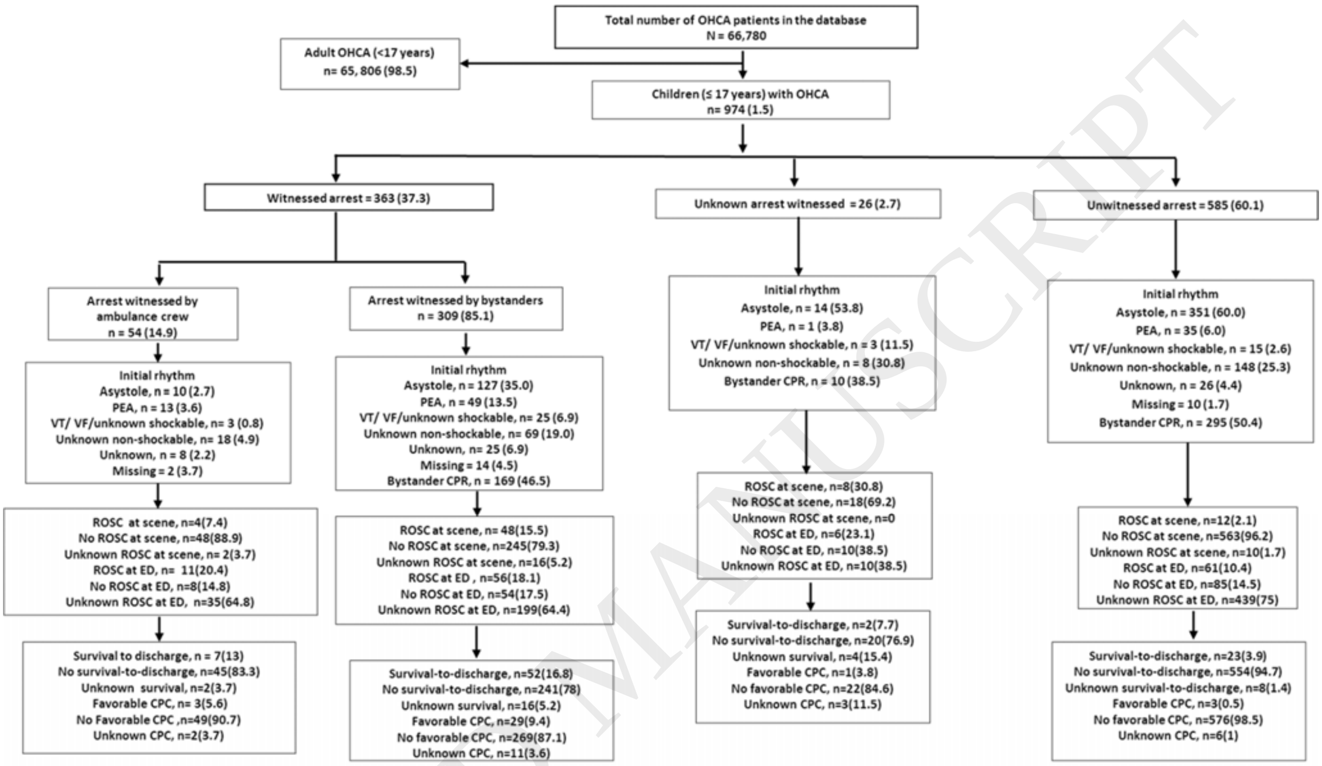

Table 1: Baseline Characteristics of included Paediatric OHCA Cases

Characteristics	Japan N = 692	Korea N = 155	Malaysia N = 5	Singapore N = 59	Taiwan N = 22	Thailand N = 24	UAE N = 17	Overall N = 974
Age, years								
Median (IQR)	1.50 (0-12.5)	4 (1-14)	15 (7-15)	2 (0-10)	5 (1-13)	3.50 (1.5-13)	7 (4-12)	2 (0-12)
Gender, male (%)	413 (59.7)	104 (67.1)	3 (60.0)	30 (50.8)	14 (63.6)	13 (54.2)	13 (76.5)	590 (60.6)
Any Past Medical History[1,] (%)	14 (7.3)	5 (3.2)	0 (0.0)	28 (47.5)	4 (18.2)	5 (20.8)	4 (23.5)	60 (12.6)
Unknown0 medical history(%	179 (92.7)	61 (39.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	240 (50.5)
Transportation(%)								
EMS	692 (100)	155 (100)	5 (100)	47 (79.7)	22 (100)	6 (25)	17 (100)	944 (96.9)
Non-EMS	0 (0.0)	0 (0.0)	0 (0.0)	12 (20.3)	0 (0.0)	18 (75.0)	0 (0.0)	30 (3.1)
Location Type[1](%)								
Home residence	139 (72.0)	106 (68.4)	3 (60.0)	42 (71.2)	14 (63.6)	8 (33.3)	9 (52.9)	321 (67.6)
Healthcare facility	1 (0.5)	11 (7.1)	0 (0.0)	2 (3.4)	0 (0.0)	1 (4.2)	1 (5.9)	16 (3.4)
Public/commercial building	10 (5.2)	9 (5.8)	1 (20.0)	1 (1.7)	4 (18.2)	3 (12.5)	4 (23.5)	32 (6.7)
Nursing home	0 (0.0)	2 (1.5)	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.6)
Street/highway	15 (7.8)	9 (5.8)	1 (20.0)	4 (6.8)	4 (18.2)	4 (16.7)	2 (11.8)	39 (8.2)
Industrial place	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (8.3)	0 (0.0)	2 (0.4)
Place of recreation	0 (0.0)	4 (2.6)	0 (0.0)	3 (5.1)	0 (0.0)	0 (0.0)	1 (5.9)	8 (1.7)
In EMS/private ambulance	9 (4.7)	3 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	5 (20.8)	0 (0.0)	17 (3.6)
Other	19 (9.8)	8 (5.2)	0 (0.0)	6 (10.2)	0 (0.0)	1 (4.2)	0 (0.0)	34 (7.2)
Arrest Witnessed By(%)								
Not witnessed	457 (66.0)	63 (40.6)	1 (20.0)	35 (59.3)	13 (59.1)	5 (20.8)	11 64.7)	585 (60.1)
EMS/private ambulance	39 (5.6)	5 (3.2)	3 (60.0)	0 (0.0)	1 (4.5)	6 (25.0)	0 (0.0)	54 (5.5)
Bystander - healthcare provider	0 (0.0)	10 (6.5)	0 (0.0)	3 (5.1)	0 (0.0)	1 (4.2)	0 (0.0)	14 (1.4)
Bystander - lay person	69 (10.0)	21 (13.5)	0 (0.0)	1 (1.7)	1 (4.5)	3 (12.5)	2 (11.8)	97 (10.0)
Bystander - family	127 (18.4)	32 (20.6)	1 (20.0)	20 (33.9)	5 (22.7)	9 (37.5)	4 (23.5)	198 (20.3)
Unknown	0 (0)	24 (15.5)	0 (0)	0 (0)	2 (9.1)	0 (0)	0 (0)	26 (2.7)
First arrest rhythm(%)								
VF/ VT	20 (2.9)	14 (9.0)	0 (0.0)	2 (4.2)	2 (9.1)	0 (0.0)	1 (5.9)	39 (4.1)
PEA	75 (10.8)	12 (7.7)	0 (0.0)	8 (16.7)	2 (9.1)	0 (0.0)	1 (5.9)	98 (10.3)
Asystole	360 (52)	83 (53.5)	2 (66.7)	33 (68.8)	8 (36.4)	1 (9.1)	15 (88.2)	502 (53.0)

Unknown shockable rhythm	5 (0.7)	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.7)
Unknown unshockable rhythm	225 (32.5)	5 (3.2)	0 (0.0)	4 (8.3)	1 (4.5)	0 (0.0)	0 (0.0)	235 (24.8)
Unknown	7 (1.0)	39 (25.2)	1 (33.3)	1 (2.1)	9 (40.9)	10 (90.9)	0 (0.0)	67 (7.1)
Dextrose	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (76.5)	13 (1.3)
Final status at scene(%)								
Pronounced dead at scene	0 (0.0)	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)	4 (0.4)
Conveyed to ED	692 (100.0)	155 (100.0)	2 (40.0)	59 (100.00)	22 (100.0)	23 (95.8)	17 (100.0)	970 (99.6)
Cardiac rhythm on arrival at ED[1](%)								
VF/ VT/ unknown shockable rhythm	13 (6.8)	5 (3.2)	0 (0.0)	4 (6.8)	3 (13.6)	1 (4.2)	1 (5.9)	27 (5.7)
PEA	152 (78.8)	12 (7.7)	0 (0.0)	8 (13.6)	0 (0.0)	2 (8.3)	1 (5.9)	175 (36.8)
Asystole	28 (14.5)	105 (67.7)	1 (20.0)	47 (79.7)	17 (77.3)	20 (83.3)	15 (88.2)	233 (49.1)
Sinus or other perfusing rhythm	0 (0.0)	27 (17.4)	0 (0.0)	0 (0.0)	2 (9.1)	0 (0.0)	0 (0.0)	29 (6.1)
Cause of arrest(%)								
Trauma	192 (27.8)	34 (21.9)	2 (40.0)	4 (6.8)	3 (13.6)	7 (29.2)	4 (23.5)	246 (25.3)
Presumed cardiac etiology	248 (35.8)	45 (29.0)	1 (20.0)	18 (30.5)	15 (68.2)	1 (4.2)	5 (29.4)	333 (34.2)
Respiratory	36 (5.2)	2 (1.3)	0 (0.0)	15 (25.4)	2 (9.1)	9 (37.5)	0 (0.0)	64 (6.6)
Electrocution	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)	1 (0.1)
Drowning	13 (1.9)	3 (1.9)	1 (20.0)	6 (10.2)	1 (4.5)	3 (12.5)	2 (11.8)	29 (3.0)
Other	203 (29.3)	71 (45.9)	1 (20.0)	16 (27.1)	1 (4.5)	3 (12.5)	6 (35.3)	301 (31.0)
Year range	2009-2010	2011-2012	2010-2012	2010-2012	2010-2011	2010-2012	2011-2012	

[1]Data not available from Tokyo and Aichi therefore total n for Japan equals 193,IQR; Interquartile range

Table 2 Pre-hospital interventions of included Paediatric OHCA cases

Characteristics ~~(%)~~	Japan N = 692	Korea N = 155	Malaysia N = 5	Singapore N = 59	Taiwan N = 22	Thailand N = 24	UAE N = 17	Overall N = 974
Bystander CPR(%)	361 (52.2)	83 (53.5)	1 (20.0)	21 (35.6)	10 (45.5)	1 (4.2)	2 (11.8)	479 (49.2)
First CPR Initiated by(%)								
No CPR initiated	0 (0.0)	0 (0.0)	1 (20.0)	8 (13.6)	0 (0.0)	12 (50.0)	0 (0.0)	21 (2.2)
First responder	7 (1.0)	0 (0.0)	0 (0.0)	2 (3.4)	0 (0.0)	1 (4.2)	0 (0.0)	10 (1.0)
Ambulance crew	223 (32.2)	72 (46.5)	3 (60.0)	28 (47.5)	12 (54.5)	10 (41.7)	15 (88.2)	279 (28.6)
Bystander - healthcare provider	0 (0.0)		0 (0.0)	5 (8.5)		1 (4.2)	1 (5.9)	7 (0.7)
Bystander - lay person	33 (4.8)	83 (53.5)[1]	0 (0.0)	5 (8.5)	10 (45.5)[1]	0 (0.0)	1 (5.9)	39 (4.0)
Bystander - family	65 (9.4)		1 (20.0)	11 (18.6)		0 (0.0)	0 (0.0)	77 (7.9)
Unknown	364 (52.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	364 (37.4)
Prehospital Defibrillation(%)	34 (4.9)	20 (12.9)	0 (0.0)	3 (5.1)	4 (18.2)	0 (0.0)	2 (11.8)	63 (6.5)
First defibrillation performed by(%)								
First responder	3 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.3)
Ambulance crew	23 (3.3)	20	0 (0.0)	3 (5.1)	4 (18.2)	0 (0.0)	2 (11.5)	52 (5.3)
Bystander - lay person	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.2)
First responder & Bystander - layperson	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.1)
Ambulance crew & Bystander - layperson	5 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.5)
Prehospital advanced airway(%)	96 (13.9)	13 (8.4)	1 (20.0)	9 (15.3)	3 (13.6)	4 (16.7)	1 (5.9)	127 (13.0)
Types of advanced airway(%)								
Oral/nasal ET	10 (1.4)	4 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	4 (16.7)	0 (0.0)	18 (1.8)
LMA	36 (5.2)	3 (1.9	0 (0.0)	9 (15.3)	3 (13.6)	0 (0.0)	1 (5.9_	52 (5.3)
King airway	25 (3.6)	2 (1.3)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	27 (2.8)
Other	25 (3.6)	4 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	29 (3.0)
Prehospital drug Administered(%)								
Epinephrine	10 (1.4)	0 (0.0)	0 (0.0)	4 (6.8)	2 (9.1)	2 (8.3)	1 (5.9)	19 (2.0)
Atropine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	1 (0.1)
Amiodarone	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.9)	1 (0.1)
Dextrose	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (76.5)	13 (1.3)

[1]; No breakdown data available for Korea and Taiwan

Tables 3: Emergency Medical Services Timings and Outcomes of included paediatric OHCA cases

	Japan N= 692	Korea N = 155	Malaysia N = 5	Singapore N = 59	Taiwan N = 22	Thailand N = 24	UAE N = 17	Overall N = 974

Time of call to time ambulance arrived at the scene[1] (minutes:seconds) median(IQR)	n=692	n=155	n =5	n =47	n =22	n =6	n =17	n =944
	6(5-7:98)	6(4-6:98)	19(16-23)	7:45(5:28-10)	6(5- 8)	8:5(5-10)	9(6-10)	6(4:9-7:9)
Time of arrival at scene to time leave scene[1,2] (minutes:seconds) **median(IQR)**	n=193	n=155	n =5	n =47	n =22	n =6	n =17	n =445
	9(7-13)	4:99(2:98-7:02)	12:78(4:02-20)	8:68(5:08-11:67)	7(3 - 11)	5(4:88-6)	9(4- 13)	7:98(4:02-11)
Prehospital ROSC (%)	44(6.4)	20(12.9)	0(0)	2(3.4)	3(13.6)	2(8.3)	1(5.9)	72 (7.4)
ED ROSC[3] **(%)**	49(7.1)	48(31)	0(0)	15(25.4)	6(27.3)	14(58.3)	2(11.8)	134 (13.8)
Survived to admission[3] **(%)**	39 (20.2)	45 (29.0)	0 (0.0)	16 (27.1)	2 (9.1)	13 (54.2)	2 (11.8)	117 (12)
Survived to discharge (%)	62 (9.0)	15 (9.7)	0 (0.0)	2 (3.4)	2 (9.1)	2 (8.3)	1 (5.9)	84 (8.5)
Unknown (%)	0(0)	22(14.2)	4(80)	2(3.4)	1(4.5)	1(4.2)	0(0)	30 (3.1)
Post arrest CPC 1-2 (%)	25 (3.6)	8 (5.2)	0 (0.0)	1 (1.7)	2 (9.1)	0 (0.0)	1 (5.9)	36 (3.7)
Unknown CPC (%)	3(0.4)	9(5.8)	4(80)	3(5.1)	1(4.5)	2(8.3)	0(0)	22 (2.3)

[1]Time arrival at scene (min): time interval computation will use the earliest arrived at scene timing from either first responder or ambulance

[2]Time leave scene (min): data not available from Tokyo and Aichi

[3]Data not available from Tokyo and Aichi therefore total n for Japan equals 193 and overall n equals to 475

IQR; Interquartile range

Table 4: Pre- hospital Factors associated with Survival to Discharge

Variable	**OR(95% CI)**	**aOR(95% CI)^**
Age category		
< 1 year old	Reference	Reference
1-5 years old	1.61(0.86-2.99)	0.62(0.13-2.98)
6-12 years old	1.22(0.56-2.63)	0.43(0.06-3.37)
13-17 years old	2.43(1.35-4.4)*	0.65(0.11-3.82)
Arrest witnessed by		
Not witnessed	**Reference**	**Reference**
EMS/private ambulance	3.59(1.47-8.79)*	13.42(1.2-149.82)*
Bystander healthcare	5.13(1.05-25.05)*	14.52(0.48-436.19)
Bystander layperson	9.94(5.44-18.17)*	7.53(1.55-36.52)*
Bystander family	3.46(1.92-6.21)*	13.14(3.32-52.07)*
Bystander CPR	1.55(0.99-2.42)	1.66(0.52-5.23)
First rhythm		
Asystole	**Reference**	**Reference**
VF,VT,Unknown shockable rhythms	20.29(9.45-43.57)*	85.49(2.64-2763.66)*
PEA, Unknown unshockable rhythms	3.59(1.99-6.47)*	8.49(0.97-74.67)
Prehospital defibrillation	5.36(2.96-9.72)*	2.37(0.15-37.06)
Prehospital advanced airway	1.18(0.63-2.19)	1.69(0.39-7.39)
Prehospital drug administration	2.17(0.87-5.4)	1.14(0.14-9.37)
Time between call and ambulance arriving at scene	0.99(0.93-1.06)	0.81(0.65-1.02)
Time between ambulance arriving at scene and leaving scene	1.01(0.96-1.05)	0.92(0.8-1.04)
Cause of arrest		
Trauma	**Reference**	**Reference**
Presumed cardiac etiology	1.5(0.81-2.76)	2.11(0.23-19.27)
Non-cardiac etiology (Respiratory, Electrocution, Drowning, Other)	1.49(0.82-2.7)	8.89(0.96-82.38)

OR; Odds ratio, 95% CI;95% confidence interval, aOR; Adjusted Odds ratio, ^;Multivariate analysis adjusted for Age, Arrest witnessed by, First rhythm, Prehospital defibrillation, Prehospital advanced airway, Prehospital drug administration, Time between call and ambulance arriving at scene, Time between ambulance arriving at scene and leaving scene, *; Statistically significant($p<0.05$)

Table 5: Pre- hospital Factors associated with Survival to Discharge (Age groups <13, >=13)

Variable	**Age<13 (n=578) aOR(95% CI)^**	**Age>=13 (n=396) aOR(95% CI)^**
Age category		
< 1 year old	**Reference**	
1-5 years old	1.23(0.58-2.57)	
6-12 years old		**Reference**
13-17 years old		1.67(0.65-4.28)
Arrest witnessed by	Arrest witnessed by	
Not witnessed	**Reference**	**Reference**
EMS/private ambulance	9.26(2.07-41.36)*	4.35(0.81-23.33)
Bystander healthcare	3.95(1.82-8.59)*	6.43(2.46-16.8)*
Bystander layperson		
Bystander family		
Bystander CPR	1.12(0.52-2.42)	2.74(1.03-7.3)*
First rhythm		
Asystole	**Reference**	**Reference**
VF,VT,Unknown shockable rhythms	3.03(0.41-22.54)	20.51(2.15-195.7)*
PEA, Unknown unshockable rhythms	Reference	Reference
Prehospital defibrillation	1.67(0.1-29.21)	0.48(0.05-4.28)
Prehospital advanced airway	3.35(1.23-9.13)*	0.4(0.13-1.26)
Prehospital drug administration	0.9(0.08-10.26)	1.06(0.23-4.79)
Time between call and ambulance arriving at scene	0.98(0.85-1.12)	0.93(0.8-1.09)
Time between ambulance arriving at scene and leaving scene		
Cause of arrest		
Trauma	**Reference**	**Reference**
Presumed cardiac etiology	0.71(0.23-2.23)	1.53(0.51-4.59)
Non-cardiac etiology (Respiratory, Electrocution, Drowning, Other)	1.2(0.42-3.48)	2.69(0.9-8)

OR; Odds ratio, 95% CI;95% confidence interval, aOR; Adjusted Odds ratio, ^;Multivariate analysis adjusted for Age, Arrest witnessed by, First rhythm, Prehospital defibrillation, Prehospital advanced airway, Prehospital drug administration, Time between call and ambulance arriving at scene, Time between ambulance arriving at scene and leaving scene, *; Statistically significant($p<0.05$)