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Regional Variation in Survival Following Pediatric Out-of-Hospital Cardiac Arrest

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Background: Although regional variation in outcome after adult out-of-hospital cardiac arrest (OHCA) is known, no clinical studies have assessed this in pediatric OHCA.

Methods and Results: This nationwide, prospective, population-based observation of the whole of Japan included consecutive OHCA patients with resuscitation attempt from January 2005 through December 2009. Primary outcome was 1-month survival with neurologically favorable outcome. Japan was divided into the following 7 regions as the largest administrative units: Hokkaido-Tohoku, Kanto, Tokai-Hokuriku, Kinki, Chugoku, Shikoku, and Kyushu-Okinawa. The outcome of pediatric OHCA was then compared between the regions. Multiple logistic regression analysis was used to adjust for other factors that were considered to influence the relationship between region and outcome. A total of 8,240 pediatric OHCA patients were registered during the study period. One-month survival with neurologically favorable outcome significantly differed by region: 2.5% (24/967) in Hokkaido-Tohoku (adjusted odds ratio [AOR], 1.65; 95% confidence interval [CI]: 0.94–2.90), 2.9% (47/1614) in Tokai-Hokuriku (AOR, 2.06; 95% CI: 1.28–3.31), 2.1% (26/1239) in Kinki (AOR, 1.45; 95% CI: 0.84–2.51), 3.4% (16/465) in Chugoku (AOR, 3.11; 95% CI: 1.62–6.00), 1.5% (4/259) in Shikoku (AOR, 0.79; 95% CI: 0.26–2.43), and 2.8% (27/974) in Kyushu-Okinawa (AOR, 2.15; 95% CI: 1.24–3.74) referred to Kanto (1.4%, 37/2722).

Conclusions: According to Japanese nationwide OHCA registry data there are significant regional variations in the outcome of pediatric OHCA. (*Circ J* 2013; **77:** 2596–2603)

Key Words: Cardiopulmonary resuscitation; Children; Out-of-hospital cardiac arrest; Regional variation; Utstein

Approximately 2,000 out-of-hospital cardiac arrests (OHCAs) occur annually among children in Japan.[1,2] Recently, some studies have reported that the characteristics and outcomes of pediatric OHCA differ from those of adults,[3–6] and children are more likely to survive an OHCA than adults, although the proportion is still low.[7] There might be some child-specific circumstances and countermeasures.

Editorial p 2475

The preceding studies found that OHCA outcome varied by geographic region for adults.[8–11] Difference in the quality and quantity of the emergency medical service (EMS) systems might be a possible explanation for the regional variation.[8,9] For children, regional variation in OHCA outcome might be greater because treatment for pediatric OHCA is more specific and more complicated, and require much greater expertise than for adult OHCA,[12] but no clinical studies have addressed these questions.

The All-Japan Utstein Registry is a large prospective population-based cohort study of OHCA in Japan, which was launched in 2005 and covers approximately 127 million residents.[1,2,13] During the 5 years beginning 2005, there have been approximately 10,000 resuscitated OHCAs in children. Using this nationwide database, we evaluated regional variations in outcome of pediatric OHCA.

Methods

Study Design and Settings

The All-Japan Utstein registry of the Fire and Disaster Management Agency (FDMA) is a prospective, nationwide, pop-

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ulation-based registry system of OHCA in adults and children, with Utstein-style data collection.[14,15] This study enrolled all adult and pediatric patients who had an OHCA, were treated by EMS personnel, and were transported to medical institutions from 1 January 2005 through 31 December 2009. The research protocol was approved by the Ethics Committee of Kyoto University Graduate School of Medicine, and the requirement of informed consent was waived according to the national ethics guidelines for epidemiological studies established by the Japanese government.

Cardiac arrest was defined as the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation.[14,15] The arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular disease, respiratory disease, malignant tumor, external causes including trauma, hanging, drowning, drug overdose, and asphyxia, or any other non-cardiac cause. Diagnosis of presumed cardiac or non-cardiac origin was clinically made by the physician in charge, in collaboration with the EMS personnel.

Do-not-resuscitate orders or living wills are generally not accepted in Japan, and EMS providers are not legally permitted to terminate resuscitation in the field. Therefore, most patients with OHCA treated by EMS personnel were transported to hospital and registered in this cohort. The cohort excluded cases of obvious signs of death on EMS arrival such as decapitation, incineration, decomposition, rigor mortis, or dependent lividity.

EMS Systems in Japan

Japan had a population of approximately 127 million in 2005, 21.3 million of whom were <18 years of age in an area of approximately 378,000 km^2 (inhabited area, 121,000 km^2).[16] EMS is provided by municipal governments through a fire department model. There were 804 fire departments with a respective dispatch center in 2009. Usually, a fire department ambulance has a crew of 3 emergency providers, including at least 1 emergency life-saving technician (ELST). ELSTs are trained to insert an i.v. line, place an adjunct airway, and use a semi-automated external defibrillator. Under online medical control, specially trained ELSTs have also been able to insert an endotracheal tube, and give i.v. epinephrine since April 2006.[17] Citizen use of automated external defibrillator (AED) has been legally permitted since July 2004 in Japan.[18] All EMS providers perform cardiopulmonary resuscitation (CPR) according to the Japanese CPR guidelines, which are based on the European Resuscitation Council and American Heart Association guidelines, and the International Liaison Committee on Resuscitation (ILCOR) recommendations.[3–6] In Japan, approximately 2 million citizens per year participate in community CPR programs, which includes training in chest compression, mouth-to-mouth ventilation, and use of AED.[1]

Data Collection and Quality Control

Data were collected with the use of a form based on the Utstein-style guidelines for reporting OHCA,[14,15] and included details on sex, age, witness status, first recorded cardiac rhythm, time course of resuscitation, bystander-initiated CPR, public-access AED use, advanced airway management, i.v. epinephrine, as well as pre-hospital return of spontaneous circulation (ROSC), 1-month survival, and neurological status 1 month after the event. The time course of resuscitation included details on the time of call received, vehicle arrival at the scene, contact with patient, initiation of CPR, defibrillation by EMS, and hospital arrival. First documented rhythm was recorded and diagnosed by the EMS personnel with semi-automated defibrillators on the scene. When laypersons delivered shocks using a public-access AED, the victims' first documented rhythm was regarded as ventricular fibrillation (VF). Both bystander-initiated chest compression-only and conventional CPR with rescue breathing were considered as bystander CPR. The time of collapse and initiation of bystander CPR was obtained by EMS interview with the bystander before leaving the scene. The time of defibrillation by EMS personnel was recorded in the semi-automated defibrillator. All survivors were evaluated 1 month after the event for their neurological function by the EMS personnel in charge.

The data form was filled out by the EMS personnel in cooperation with the physicians in charge of the patients, and the data were integrated into the registry system on the FDMA database server. They were logically checked by the computer system and were confirmed by the implementation working group. If the data form was incomplete, the FDMA returned it to the respective fire station for completion.

Key Regional Definition and Demographic Data

To assess regional variations in OHCA, we divided Japan into the following 7 regions as the largest administrative units in Japan: Hokkaido-Tohoku, Kanto, Tokai-Hokuriku, Kinki, Chugoku, Shikoku, and Kyushu-Okinawa, which are commonly used in administrative surveys.[19] We obtained the following information by region: pediatric and adult population and the densities (per 1,000 km^2 inhabited area) of pediatricians, emergency pediatricians, hospitals, EMS personnel, and ambulances calculated from Japanese administrative materials.[1,20]

Main Outcome Measure

Neurological outcome was assessed with the Glasgow-Pittsburgh Cerebral Performance Category (CPC) scale as: 1, good performance; 2, moderate disability; 3, severe cerebral disability; 4, coma/vegetative state; and 5, death. The primary outcome measure was 1-month survival with favorable neurological outcome, defined as CPC category 1 or 2.[2,14,15] Secondary outcome measures included pre-hospital ROSC and 1-month survival.

Statistical Analysis

The characteristics of patients and prehospital care in pediatric OHCA were compared among the 7 regions using analysis of variance for numerical variables, and chi-squared test or Fisher's exact test for categorical variables. Multivariate analysis was used to assess the regional variation for 1-month survival with favorable neurological outcome; adjusted odds ratios (AORs) and their 95% confidence intervals (CIs) were calculated. As potential confounders, factors that were biologically essential and considered to be associated with clinical outcome were used in multivariate analysis. These variables included age (infants aged <1 year; children aged 1–17 years); sex (male, female); origin of arrest (cardiac, non-cardiac); type of bystander witness (none, family members and others); first documented rhythm (VF, non-VF); type of bystander-initiated CPR (none, any CPR); time interval from call to CPR by EMS personnel (for 1-min increments); and year of arrest (for 1-year increments). In addition, we calculated the AORs of OHCA children for neurologically favorable outcome referring to adults in the respective region by multivariate logistic regression analysis.

All of the tests were 2-tailed and $P<0.05$ was considered statistically significant. All statistical analysis was done using SPSS version 16.0J (SPSS, Chicago, IL, USA).

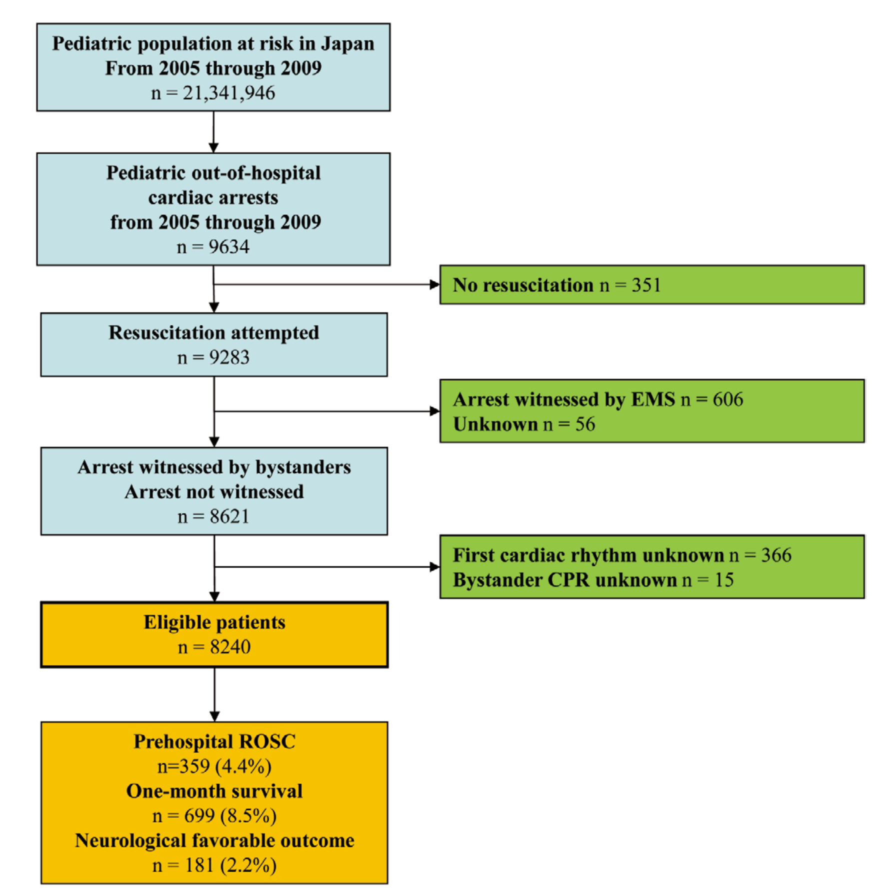

Figure 1. Study flow of pediatric out-of-hospital cardiac arrest cases with an abridged Utstein template from 1 January 2005 through 31 December 2009. CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ROSC, return of spontaneous circulation.

Table 1. Pediatric OHCA Demographic Characteristics by Region in Japan

	Hokkaido-Tohoku	Kanto	Tokai-Hokuriku	Kinki	Chugoku	Shikoku	Kyushu-Okinawa
Pediatric population (×1,000)	2,540	6,542	4,120	3,514	1,299	675	2,651
Population density†	60	361	180	415	155	139	161
Density‡ of							
Pediatricians	34.7	272.8	105.4	299.6	109.0	101.2	106.4
Emergency physicians	27.8	180.8	70.3	212.7	72.7	63.9	91.4
Hospitals	12.9	55.8	29.5	78.4	36.1	37.1	32.6
EMS personnel	256.7	675.8	592.9	946.7	619.5	456.6	415.5
Ambulances	23.7	80.9	52.3	96.7	56.6	52.5	45.7
Incidence§ (95% CI)							
Age 0–17 years	7.6 (6.3–8.9)	8.3 (6.8–9.8)	7.8 (6.7–8.9)	7.1 (6.7–7.4)	7.2 (6.3–8.0)	7.7 (6.1–9.3)	7.4 (6.9–7.8)
Age 1–17 years	4.8 (4.1–5.0)	4.6 (3.9–4.7)	4.6 (4.1–4.7)	4.6 (4.1–4.6)	4.7 (3.9–5.0)	4.9 (4.2–5.2)	4.8 (4.2–5.0)
Age <1 year	67.6 (43.8–91.2)	77.4 (45.6–109.2)	69.2 (45.5–92.9)	54.3 (50.9–57.7)	55.9 (44.4–67.4)	63.7 (35.7–91.7)	57.8 (43.5–72.1)

†No. children per 1 km² inhabited area; ‡No. per 1,000 km² inhabited area; §mean annual incidence per 100,000 population. CI, confidence interval; EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest.

Results

A total of 9,634 pediatric OHCAs were documented during these 5 years in Japan (Figure 1). Out of 9,283 patients with resuscitation attempt, 8,240 who had suffered cardiac arrest before EMS arrival were enrolled in the present analysis, excluding patients with missing data on first documented rhythm (n=366) and bystander CPR (n=15). The proportion of prehospital ROSC among the eligible patients was 4.4%, 1-month survival 8.5%, and 1-month survival with neurologically favorable outcome, 2.2%.

Table 1 lists the demographic characteristics of pediatric OHCA by region. The population density and the densities of pediatricians, emergency pediatricians, hospitals, EMS personnel, and ambulances substantially differed among the 7 regions. The annual incidence of pediatric OHCA per 100,000

Table 2. Pediatric OHCA Patient and EMS Characteristics by Region in Japan

	Hokkaido-Tohoku (n=967)	Kanto (n=2,722)	Tokai-Hokuriku (n=1,614)	Kinki (n=1,239)	Chugoku (n=465)	Shikoku (n=259)	Kyushu-Okinawa (n=974)	P-value‡
Age (years)	2 (0–12)	1 (0–9)	1 (0–11)	2 (0–11)	2 (0–11)	2 (0–12)	2 (0–11)	<0.001
Infant aged <1 year	391 40.4 (37.3–43.6)	1,310 48.1 (46.2–50.0)	707 43.8 (41.4–46.3)	477 38.5 (35.8–41.3)	177 38.1 (33.6–42.7)	101 39.0 (33.0–45.2)	369 37.9 (34.8–41.0)	<0.001
Male	605 62.6 (59.4–65.6)	1,647 60.5 (58.6–62.4)	998 61.8 (59.4–64.2)	746 60.2 (57.4–63.0)	280 60.2 (55.6–64.7)	142 54.8 (48.6–61.0)	597 61.3 (58.2–64.4)	0.390
Type of origin								<0.001
Cardiac origin	301 31.1 (28.2–34.2)	1,013 37.2 (35.4–39.1)	510 31.6 (29.3–33.9)	407 32.8 (30.2–35.5)	98 21.1 (17.5–25.1)	92 35.5 (29.7–41.7)	195 20.0 (17.6–22.7)	
Non-cardiac origin	666 68.9 (65.9–71.8)	1,709 62.8 (60.9–64.6)	1,104 68.4 (66.1–70.7)	832 67.2 (64.5–70.0)	367 78.9 (74.9–82.6)	167 64.5 (58.3–70.3)	779 80.0 (77.3–82.5)	
Type of bystander-witnessed status								0.086
No witness	696 72.0 (69.0–74.8)	2,005 73.7 (72.0–75.3)	1,175 72.8 (70.6–75.0)	923 74.5 (72.0–77.0)	348 74.8 (70.6–78.7)	192 74.1 (68.4–79.4)	720 73.9 (71.0–76.7)	
Family	170 17.6 (15.2–20.1)	431 15.8 (14.5–17.3)	271 16.8 (15.0–18.7)	172 13.9 (12.0–15.9)	59 12.7 (9.8–16.1)	36 13.9 (9.9–18.7)	157 16.1 (13.9–18.6)	
Others	101 10.4 (8.6–12.6)	286 10.5 (9.4–11.7)	168 10.4 (9.0–12.0)	144 11.6 (9.9–13.5)	58 12.5 (9.6–15.8)	31 12.0 (8.3–16.6)	97 10.0 (8.2–12.0)	
Type of bystander-initiated CPR								<0.001
No CPR	461 47.7 (44.5–50.9)	1,523 55.9 (54.1–57.8)	800 49.6 (47.1–52.0)	634 51.2 (48.4–54.0)	244 52.5 (47.8–57.1)	134 51.8 (45.5–58.0)	428 44 (40.8–47.1)	
Chest compression-only CPR	231 23.9 (21.1–26.7)	555 20.4 (18.9–22.0)	402 24.9 (22.8–27.1)	194 15.7 (13.7–17.8)	86 18.5 (15.1–22.3)	40 15.4 (11.3–20.4)	237 24.3 (21.7–27.2)	
Conventional CPR with rescue breathing	275 28.4 (25.6–31.4)	644 23.7 (22.1–25.3)	412 25.5 (23.4–27.7)	411 33.2 (30.6–36.0)	135 29.0 (24.9–33.4)	85 32.8 (27.1–38.9)	309 31.7 (28.8–35.0)	
Type of first recorded rhythm								0.263
VF	58 6.0 (4.6–7.7)	120 4.4 (3.7–5.3)	96 6.0 (4.8–7.2)	56 4.5 (3.4–5.8)	30 6.5 (4.4–9.1)	18 7.0 (4.2–10.8)	53 5.4 (4.1–7.1)	
PEA	135 14 (11.8–16.3)	388 14.3 (13.0–15.6)	252 15.6 (13.9–17.5)	187 15.1 (13.1–17.2)	67 14.4 (11.3–17.9)	32 12.4 (8.6–17.0)	134 13.8 (11.7–16.1)	
Asystole	774 80 (77.4–82.5)	2,214 81.3 (80.0–82.8)	1,266 78.4 (76.4–80.4)	996 80.4 (78.1–82.6)	368 79.1 (75.2–82.8)	209 80.6 (75.4–85.3)	787 80.8 (78.2–83.2)	
Public-access AED use	3 0.3 (0.1–0.9)	17 0.6 (0.40–1.0)	12 0.7 (0.4–1.3)	5 0.4 (0.1–0.9)	2 0.4 (0.1–1.5)	0 0.0	2 0.2 (0.0–0.7)	0.336
Shocks by EMS†	45 4.7 (3.4–6.2)	90 3.3 (2.7–4.1)	69 4.3 (3.3–5.4)	42 3.4 (2.5–4.6)	17 3.7 (2.1–5.8)	14 5.4 (3.0–8.9)	39 4.0 (2.9–5.4)	0.383
Epinephrine use	25 2.6 (1.7–3.8)	56 2.1 (1.6–2.7)	31 1.9 (1.3–2.7)	13 1.0 (0.6–1.8)	4 0.9 (0.2–2.2)	1 0.4 (0.0–2.1)	2 0.2 (0.0–0.7)	<0.001
Intubation	13 1.3 (0.7–2.3)	64 2.4 (1.8–3.0)	32 2.0 (1.4–2.8)	24 1.9 (1.3–2.9)	5 1.1 (0.4–2.5)	5 1.9 (0.6–4.5)	16 1.6 (0.9–2.7)	<0.001
Time course by EMS (min)								
Call to CPR by EMS	9.7 (6–10)	8.9 (6–10)	9.3 (7–11)	8.3 (6–10)	9.3 (6–11)	9.1 (6–10)	9.4 (6–11)	<0.001
Call to hospital arrival	30.7 (20–37)	31.0 (23–36)	29.2 (20–34)	27.8 (20–32.5)	28.6 (19–33)	27.8 (18–32)	26.7 (18–31)	<0.001

Data given as median (IQR), or n % (95% CI). †Calculated only for VF cases. ‡Calculated to test the homogeneity among the 7 regional groups. AED, automated external defibrillation; CPR, cardiopulmonary resuscitation; IQR, interquartile range; PEA, pulseless electrical activity; VF, ventricular fibrillation. Other abbreviations as in Table 1.

Table 3. Pediatric OHCA Outcome by Region in Japan

	Hokkaido-Tohoku (n=967)	Kanto (n=2,722)	Tokai-Hokuriku (n=1,614)	Kinki (n=1,239)	Chugoku (n=465)	Shikoku (n=259)	Kyushu-Okinawa (n=974)
Prehospital ROSC, n (%)	47 (4.9)	108 (4.0)	77 (4.8)	54 (4.3)	21 (4.5)	9 (3.5)	43 (4.4)
Crude OR (95% CI)	1.24 (0.87–1.76)	Reference	1.21 (0.90–1.64)	1.10 (0.79–1.54)	1.14 (0.71–1.85)	0.87 (0.44–1.74)	1.11 (0.78–1.60)
Adjusted OR (95% CI)	1.08 (0.75–1.57)	Reference	1.07 (0.78–1.46)	0.97 (0.68–1.37)	1.02 (0.62–1.68)	0.71 (0.34–1.45)	0.96 (0.66–1.40)
One-month survival, n (%)	82 (8.5)	158 (5.8)	146 (9.0)	118 (9.5)	52 (11.2)	24 (9.3)	119 (12.2)
Crude OR (95% CI)	1.51 (1.14–1.99)	Reference	1.61 (1.28–2.04)	1.71 (1.33–2.19)	2.04 (1.47–2.84)	1.66 (1.06–2.60)	2.26 (1.76–2.90)
Adjusted OR (95% CI)	1.42 (1.06–1.89)	Reference	1.54 (1.21–1.97)	1.62 (1.25–2.10)	2.0 (1.41–2.82)	1.53 (0.95–2.45)	2.16 (1.66–2.80)
Neurologically favorable 1-month survival, n (%)	24 (2.5)	37 (1.4)	47 (2.9)	26 (2.1)	16 (3.4)	4 (1.5)	27 (2.8)
Crude OR (95% CI)	1.85 (1.10–3.10)	Reference	2.18 (1.41–3.36)	1.56 (0.94–2.58)	2.60 (1.43–4.69)	1.14 (0.40–3.22)	2.07 (1.25–3.42)
Adjusted OR (95% CI)	1.65 (0.94–2.90)	Reference	2.06 (1.28–3.31)	1.45 (0.84–2.51)	3.11 (1.62–6.00)	0.79 (0.26–2.43)	2.15 (1.24–3.74)

ORs were adjusted for sex, age, origin of arrest, type of bystander witness, type of bystander CPR, first recorded rhythm, time interval from call to CPR by EMS, and year of arrest. OR, odds ratio; ROSC, return of spontaneous circulation. Other abbreviations as in Tables 1,2.

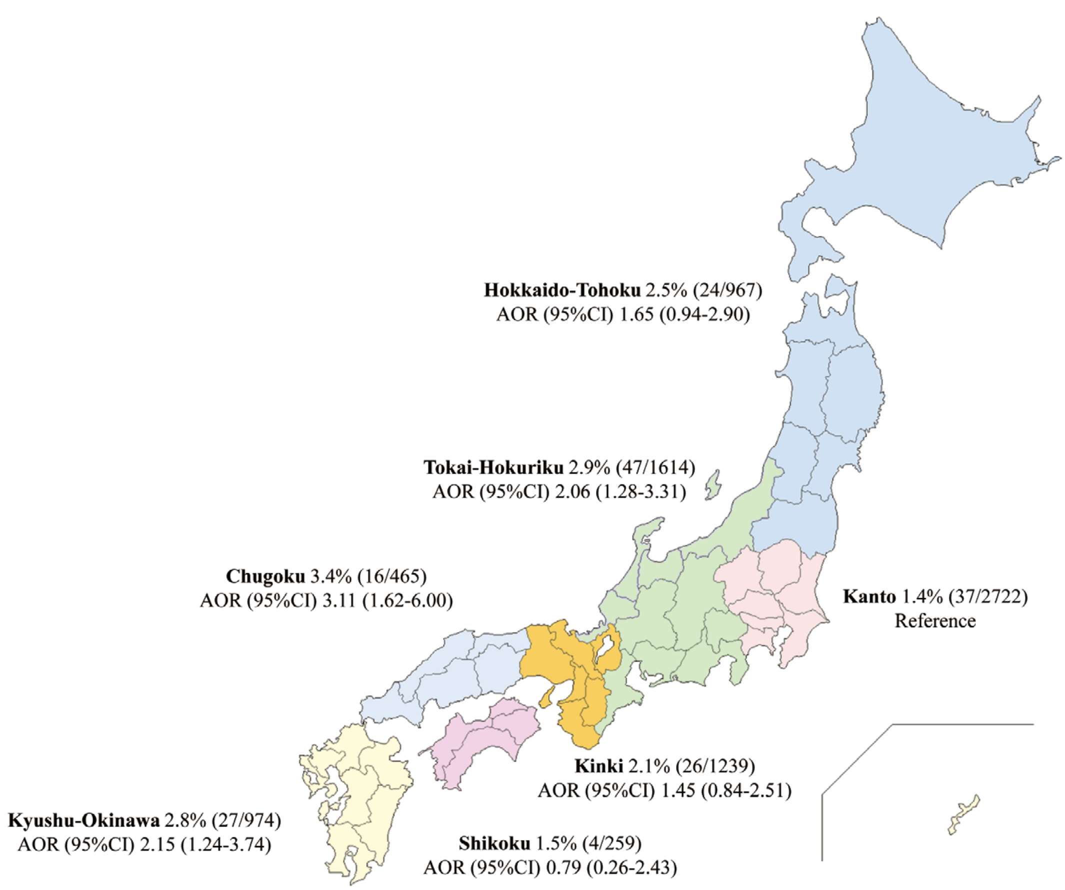

Figure 2. Proportion of neurologically favorable 1-month survival after pediatric out-of-hospital cardiac arrest in Japan according to region. Adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) compared with Kanto were calculated. ORs were adjusted for sex, age, origin of arrest, type of bystander witness, type of bystander cardiopulmonary resuscitation (CPR), first recorded rhythm, time interval from call to CPR by the emergency medical service, and year of arrest.

Table 4. One-Month Survival With Neurologically Favorable Outcome After OHCA by Region in Japan

	Hokkaido-Tohoku	Kanto	Tokai-Hokuriku	Kinki	Chugoku	Shikoku	Kyushu-Okinawa
Children	2.5 (24/967)	1.4 (37/2,722)	2.9 (47/1,614)	2.1 (26/1,239)	3.4 (16/465)	1.5 (4/259)	2.8 (27/974)
Adults	1.3 (840/64,137)	1.1 (1,773/155,389)	1.4 (1,333/95,589)	1.9 (1,338/70,714)	1.3 (343/27,100)	1.1 (171/15,080)	1.6 (798/48,986)
Crude OR (95% CI)	1.92 (1.27–2.89)	1.19 (0.86–1.66)	2.12 (1.58–2.85)	1.11 (0.75–1.65)	2.78 (1.67–4.63)	1.37 (0.50–3.71)	1.72 (1.17–2.54)
Adjusted OR (95% CI)	2.95 (1.87–4.65)	1.81 (1.28–2.56)	3.23 (2.32–4.49)	1.77 (1.16–2.72)	5.51 (3.10–9.80)	1.62 (0.56–4.68)	2.98 (1.94–4.57)

OR is for children vs. adults. ORs were adjusted for sex, age, origin of origin, type of bystander witness, type of bystander CPR, first recorded rhythm, time interval from call to CPR by EMS, and year of arrest. Abbreviations as in Tables 1–3.

Table 5. Contributing Factors to Favorable Neurological 1-Month Survival After Pediatric OHCA in Japan

	Adjusted OR (95% CI)	P-value
Male (vs. female)	0.75 (0.54–1.05)	0.099
Age 1–17 years (vs. infant aged <1 year)	1.65 (1.11–2.44)	0.012
Cardiac origin (vs. non-cardiac origin)	1.55 (1.07–2.23)	0.019
VF (vs. non-VF)	10.24 (7.04–14.91)	<0.001
Bystander-witnessed status (vs. no witness)	5.15 (3.52–7.54)	<0.001
Bystander CPR (vs. no CPR)	1.63 (1.16–2.30)	0.005
Region		
Hokkaido-Tohoku	1.65 (0.94–2.90)	0.083
Kanto	Reference	
Tokai-Hokuriku	2.06 (1.28–3.31)	0.003
Kinki	1.45 (0.84–2.51)	0.186
Chugoku	3.11 (1.62–6.00)	0.001
Shikoku	0.79 (0.26–2.43)	0.686
Kyushu-Okinawa	2.15 (1.24–3.74)	0.006
Call to CPR by EMS (for 1-min increment)	0.90 (0.85–0.95)	<0.001
Year (for 1-year increment)	1.14 (1.01–1.29)	0.030

Abbreviations as in Tables 1–3.

population ranged from 7.1 to 8.1 throughout Japan. Although the incidence was similar among the regions (4.6–4.9) for children aged 1–17 years, it varied by region (54.3–77.4) for infants aged <1 year.

The characteristics of patients and prehospital care in pediatric OHCA are noted by region in **Table 2**. Whereas the proportions of infant (37.9–48.1%) and cardiac origin (20.0–37.2%) were significantly different by region, those of witness status, VF as first recorded rhythm, public-access AED use, and shocks by EMS were similar. In contrast, the proportion of bystander CPR (44.1–56.0%) and the mean time interval from collapse to CPR by EMS (8.3–9.7 min) and to hospital arrival (26.7–31.0 min) significantly differed by region. After categorizing the data according to age group (infants aged <1 year and children aged 1–17 years; **Table S1**), there were similar regional variations in the characteristics of patients and prehospital care.

Table 3 lists the outcomes of pediatric OHCA by region. We found no significant differences in AORs for pre-hospital ROSC by region, but 1-month survival with neurologically favorable outcome was very heterogeneous (**Figure 2**), that is, significantly greater in Tokai-Hokuriku (2.9%, 47/1614; AOR, 2.06; 95% CI: 1.28–3.31), Chugoku (3.4%, 16/465; AOR, 3.11; 95% CI: 1.62–6.00), and Kyushu-Okinawa (2.8%, 27/974; AOR, 2.15; 95% CI: 1.24–3.74) compared with Kanto (1.4%, 37/2722), even adjusting for potential confounding factors. Again, after analyzing the data according to age group (infants aged <1 year and children aged 1–17 years; **Table S2**), AOR among children aged 1–17 years was significantly greater in Chugoku (AOR, 4.17; 95% CI: 1.99–8.73) and Kyushu-Okinawa (AOR, 1.98; 95% CI: 1.02–3.85) compared with Kanto. There were no significant regional differences in 1-month survival with neurologically favorable outcome after OHCA among infants aged <1 year.

The ratio of 1-month survival with neurologically favorable OHCA outcome between children and adults was compared among regions (**Table 4**). The ratios of children vs. adults were considerably different by region: 5.51 (95% CI: 3.10–9.80) in Chugoku, 3.23 (95% CI: 2.32–4.49) in Tokai-Hokuriku, 2.98 (95% CI: 1.94–4.57) in Kyushu-Okinawa, 2.95 (95% CI: 1.87–4.65) in Hokkaido-Tohoku, 1.81 (95% CI: 1.28–2.56) in Kanto, 1.77 (95% CI: 1.16–2.72) in Kinki, and 1.62 (95% CI: 0.56–4.68) in Shikoku.

On multivariate analysis (**Table 5**), compared with infants aged <1 year, children aged 1–17 years had a significantly better neurological outcome (AOR, 1.65; 95% CI: 1.11–2.44). VF as first documented rhythm (AOR, 10.24; 95% CI: 7.04–14.91), bystander-initiated CPR (AOR, 1.63; 95% CI: 1.16–2.30), and earlier CPR time by EMS (AOR for 1-min increase, 0.90; 95% CI: 0.85–0.95) were associated with better neurological outcome.

Discussion

Using the nationwide registry of OHCA in Japan, we have found that there are significant regional variation in characteristics and outcome of pediatric OHCA. In particular, we found more than 3-fold differences in neurologically favorable survival by region even considering potential known prognostic factors. In contrast to the underpowered previous studies, the present sufficiently large study has clearly identified these important regional variations in pediatric OHCA outcome. To our knowledge, this is the first report to assess the regional variation of pediatric OHCA survival.

In this study, neurologically favorable outcome significantly differed by region, whereas pre-hospital ROSC did not. This discrepancy presumably resulted from the difference in intensive care after hospital arrival. The performance and the quality of advanced life-saving treatment after hospital arrival would be the most plausible explanation for this regional variation in pediatric OHCA outcome. Recently, some studies reported that post-resuscitation care such as therapeutic hypothermia, extracorporeal CPR, and percutaneous coronary intervention might be effective for pediatric cardiac arrest.[21–24]

Differences in OHCA outcome in children were larger than those in adults. Regional variations in the pediatric health-care system such as an unbalanced density of pediatricians might be a possible reason for the regional variation. Furthermore, the pre-hospital care protocol for OHCA patients provided by the FDMA was developed mainly for adults and not for children. Given that pediatric OHCA is far less frequent than adult OHCA, then it might be difficult for both EMS personnel and physicians to accumulate sufficient experience to hone their skills for pediatric cardiac arrest. The child-specific life support system and technique should be developed and distributed.

Present multivariate analysis showed that bystander CPR was associated with better neurological outcome, and this would be a possible explanation for the poor outcome observed in the Kanto area, where the prevalence of bystander CPR was relatively low. Furthermore, the present study has shown that there were great differences in the prevalence of bystander CPRs and the resuscitation time course by the EMS by region, both of which are other key factors for OHCA survival. Many previous studies have shown that bystander CPR improved survival after pediatric and adult OHCA.[3–6,13,25,26] The difference in the prevalence of bystander CPR in this study might be derived from the difference in social activities to promote citizen CPR by region. It is well known that early CPR by EMS personnel and early access to hospitals improve survival after OHCA.[25,27] The present data showing marked regional variations in EMS response time should be discussed to establish more effective and efficient EMS systems.

Importantly, the proportion of neurologically favorable survival after pediatric OHCA remained low regardless of geographical region. Because bystander CPR and public-access AED use are not sufficiently frequent (approximately 50% and <1%, respectively) in any region, further efforts to spread CPR and AED use in communities are needed. In addition, improvements in advanced treatment for pediatric OHCA are needed. Although we previously indicated that the transportation of OHCA patients to the governmentally deployed critical care medical centers (CCMCs) contributed to improving outcome for adult OHCA,[28] it is not clear that this knowledge would be applicable to pediatric OHCA. Some reports found that transportation of OHCA children to pediatric intensive care unit (PICU) could improve their survival.[29,30] In Japan, however, most OHCA children are transported to adult CCMCs or ordinary hospitals rather than PICU. An integrated system to provide intensive care for OHCA children and an evaluation of its effectiveness are matters of urgency.

In this study, the incidence of infant OHCA and the ratio of cardiac/non-cardiac origins differed by region. Regional variations in the incidence of adult OHCA are partly explained by the regional variations in risk factors such as medication for hypertension and dyslipidemia.[8,9] A preventive approach to pediatric OHCA is important,[4] and further effort should be made to facilitate prevention of pediatric cardiac arrest.

Study Limitations

This observational study has several inherent limitations. First, we did not obtain detailed demographic and socioeconomic status, which would influence regional variations in OHCA,[31,32] and there might be unmeasured confounding factors that might have influenced the association between region and outcome. Second as with all epidemiologic studies, the integrity and validity of the data, as well as ascertainment bias, are potential limitations of the study. The use of uniform data collection based on Utstein-style guidelines for reporting cardiac arrest, the large sample size, and the population-based design should minimize these potential sources of bias.

In future studies, we will investigate detailed data including regional and social conditions such as education for citizen and hospital information in order to assess clearly the causes of the regional variations in survival following pediatric OHCA.

Conclusions

This nationwide population-based observational study has shown that there are significant regional variations in 1-month survival with neurologically favorable outcome in pediatric OHCA. To evaluate factors contributing to better outcome, further study including data on both pre- and in-hospital advanced care, and emergency transportation systems are needed.

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Supplementary Files

Supplementary File 1

Table S1. Patient and EMS Pediatric OHCA Characteristics by Region in Japan and Age Group

Table S2. Pediatric OHCA Outcome by Region in Japan and Age Group

Please find supplementary file(s);
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