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Clinical paper

# Association of bystander cardiopulmonary resuscitation and neurological outcome after out-of-hospital cardiac arrest due to drowning in Japan, 2013–2016

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## Abstract

**Background:** Early initiation of cardiopulmonary resuscitation (CPR) performed by bystanders is essential in patients with out-of-hospital cardiac arrest (OHCA) due to primary cardiac cause. However, evidence about the effect of bystander CPR on neurologically favorable survival after OHCA due to drowning is scarce and controversial.

**Methods:** This nationwide population-based observational study using prospectively collected government-led registry data included patients with OHCA due to drowning who were transported to an emergency hospital between 2013 and 2016. The primary outcome was one-month neurologically favorable survival defined as Glasgow-Pittsburgh Cerebral Performance Category score of 1-2. The secondary outcomes were one-month survival and prehospital return of spontaneous circulation (ROSC).

**Results:** The full cohort (n = 12,139) comprised 6291 (51.8%) male patients, and the mean age was 73.7 (standard deviation [SD], 18.8). Of these, 5157 (42.5%) received bystander CPR, and 6982 (57.5%) did not. 4345 patients receiving bystander CPR were propensity-matched with 4345 patients not receiving bystander CPR. In the propensity score-matched cohort, bystander CPR was associated with increased chance of one-month neurologically favorable survival (0.4% vs. 0.8%; risk ratio [RR], 2.19; 95%confidence interval [CI], 1.21–3.95; $P = 0.0076$), one-month survival (1.1% vs. 1.7%; RR, 1.55; 95%CI, 1.09–2.22; $P = 0.0150$), and prehospital ROSC (2.7% vs. 3.5%; RR, 1.30; 95%CI, 1.03–1.65; $P = 0.0296$). Similar association was observed across a variety of sensitivity analyses. In subgroup analysis, statistically significant difference was not observed in pediatric OHCA due to drowning, although the sample size was too small (n = 218).

**Conclusions:** Among patients with OHCA due to drowning, bystander CPR was associated with increased chance of neurologically favorable survival.

**Keywords:** Out-of-hospital cardiac arrest, Cardiopulmonary resuscitation, Drowning, Basic life support, Epidemiology

*Abbreviations:* AHA, American Heart Association; ALS, advanced life support; BLS, Basic life support; CARES, Cardiac Arrest Registry for Enhanced Survival; CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; CI, confidence interval; DNR, do-not-resuscitate; EMS, emergency medical services; FDMA, Fire and Disaster Management Agency; IQR, interquartile range; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; PEA, pulseless electrical activity; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; RR, risk ratio; SD, standard deviation; VF, ventricular fibrillation; VT, ventricular tachycardia.

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## Introduction

Drowning is an important public health issue. Globally, about 400,000 deaths due to drowning occur each year, which account for 0.7% of all deaths worldwide.[1–3] Every minute of every day, approximately 1.5 people die from drowning in the world. In Japan, there are about 5000 to 6000 drowning deaths each year.

In out-of-hospital cardiac arrest (OHCA) due to drowning, it is essential to call for emergency medical services (EMS) immediately.[2,4–6] As with OHCA due to a primary cardiac cause, early initiation of cardiopulmonary resuscitation (CPR) is assumed to be essential in OHCA due to drowning,[2,4–7] although effective CPR may be impossible to initiate until the drowned patient is rescued and is taken to dry land.[2,8]

Thus far, no randomized controlled trial (RCT) has examined the effect of bystander CPR on OHCA due to drowning. In observational studies, most studies indicated that bystander CPR might not be associated with an increased chance of favorable outcomes after OHCA due to drowning, although the sample size was relatively small (less than 1000) in those studies.[9–13]

We sought to assess whether bystander CPR would be associated with an increased chance of neurologically favorable survival after OHCA due to drowning using the government-led registry data between 2013 and 2016.

## Materials and methods

### Data source, study setting, and participants

The All-Japan Utstein Registry is a government-led nationwide population-based registry of OHCA patients, managed by the Fire and Disaster Management Agency (FDMA). Data were collected in conformity with the Utstein-style uniform reporting for cardiac arrest,[14,15] and not the dedicated Utstein-style reporting template for drowning.[16]

As previous studies have described in detail,[17–21] data on OHCA patients transported to an emergency hospital are prospectively collected by trained EMS personnel. Almost all OHCA patients, including those with do-not-resuscitate (DNR) orders, are included in this registry because EMS personnel in Japan are not allowed to terminate out-of-hospital resuscitation except in specific situations (e.g., decapitation, rigor mortis, livor mortis, or decomposition). Data are collected from three sources (i.e., 1-1-9 dispatch centers, fire stations, and receiving hospitals). EMS personnel fill out the data forms in cooperation with the physician in charge of the patient, and the data are integrated into the All-Japan Utstein Registry system on the FDMA database server. The data integrity, accuracy, and completeness are secured through both the certification by the FDMA and the logical internal checks using standardized software. If the data form is incomplete, the FDMA return it to the respective fire station, and the form is then reconfirmed and completed.

In Japan, CPR training programs for citizens are provided by such as local fire departments and are based on the Japanese CPR guidelines, which substantially conform to the American Heart Association (AHA) CPR guidelines. It is estimated that almost four million citizens are trained in CPR annually. Telephone-assisted CPR instructed by dispatchers for bystanders was established in July 1999.[22,23]

This study included patients with OHCA due to drowning who were submitted to the All-Japan Utstein Registry between January 1, 2013 and December 31, 2016. Patients with missing or unknown data on bystander CPR and dispatcher-assisted CPR were excluded. Although both witnessed and unwitnessed OHCA patients were included, EMS personnel-witnessed OHCA patients were excluded. In addition, patients with an unrealistic or contradictory (i.e., negative or considerably long) time interval and patients with missing or unknown data on EMS activity times were excluded. Patients with missing or unknown data accounted for approximately 20% of total patients with OHCA due to drowning (Fig. 1).

This study was conducted according to the amended Declaration of Helsinki. The institutional review board of University of the Ryukyus approved this study with a waiver of informed consent due to the anonymous nature of the data (#392_H290302).

### Data collection

Data on patient characteristics (i.e., age and sex), bystander characteristics (i.e., witness, bystander CPR, and dispatcher-assisted CPR), cardiac arrest characteristics (i.e., etiology of cardiac arrest and initial rhythm), and event characteristics (i.e., time and place of cardiac arrest) were collected. Although witnessed arrest is typically defined as a cardiac arrest that is seen or heard by another person or is monitored, it is sometimes difficult to notice the moment of actual cardiac arrest in OHCA due to drowning. Thus, some witness of arrest may be based on the moment of submersion. Data on prehospital care by healthcare professionals (i.e., intravenous line insertion, epinephrine administration, advanced airway management, and physician involvement in prehospital advanced life support [ALS]) were also collected. In addition, a series of EMS activity times (i.e., emergency call, contact with patient, and hospital arrival) were recorded by each EMS squad. Time intervals were calculated based on the time variables recorded in whole minutes. When two events occurred within the same whole minute, the time interval was calculated as 0 min. Response time and transport time represent the time interval between emergency call and contact with patient and the time interval between contact with patient and hospital arrival, respectively. One-month follow-up survey was conducted by each fire department to collect outcome data on survival and neurological status, based on an inquiry for the receiving hospital. At the same time, the etiology of the cardiac arrest was reconfirmed, although the etiology of the cardiac arrest was temporarily determined by attending physicians in the emergency department in collaboration with EMS personnel on the day of the emergency transportation. The fire department conducted further investigations in cooperation with the hospital personnel, if the patient information was not acquired from the hospital because of hospital transfer or discharge within one month.

### Outcomes

The primary outcome was one-month neurologically favorable survival. Neurological outcome was assessed by inpatient attending physicians with the Glasgow-Pittsburgh cerebral performance category (CPC) scores. A CPC score of 1 (good performance) or 2 (moderate disability) was considered a favorable neurological outcome, whereas a CPC score of 3 (severe disability), 4 (vegetative state), or 5 (death) was considered a poor neurological outcome.[15,24] The secondary outcomes were one-month survival and prehospital return of spontaneous circulation (ROSC).

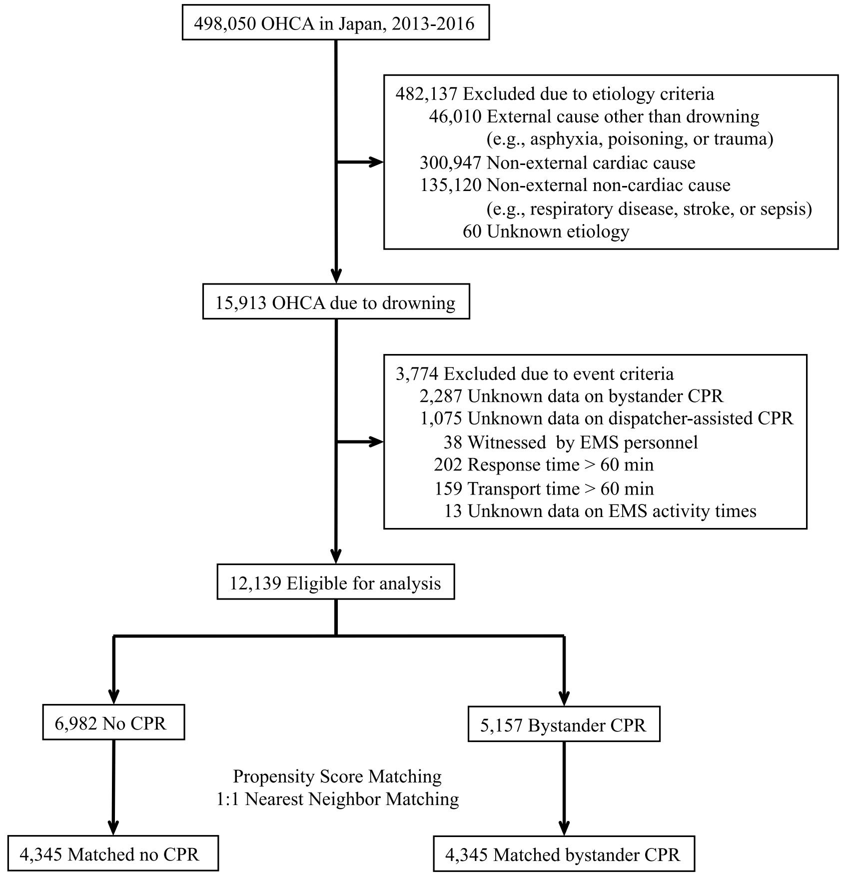


**Fig. 1 – Study flow diagram.**
**Abbreviations: CPR, Cardiopulmonary resuscitation; EMS, Emergency medical service; OHCA, Out-of-hospital cardiac arrest**

### *Statistical analysis*

Descriptive statistics were presented for the full and propensity score-matched cohort. Categorical variables were reported as counts with frequencies (%), and the $\chi^2$ test was used to compare category variables. Continuous variables were reported as means with standard deviations (SDs) or medians with interquartile ranges (IQRs).

Due to the lack of randomization, we performed propensity score-matched analyses in an effort to control for selection bias and confounding. We estimated the propensity score for each patient with or without bystander CPR using a multivariable logistic regression model. The following variables having pre-treatment characteristics were included in the model: age, sex (male or female), witness (no witness, witness by family member, or witness by non-family member), dispatcher's instruction for CPR (yes or no), initial rhythm (ventricular fibrillation [VF], ventricular tachycardia [VT], pulseless electrical activity [PEA], asystole, or others), year of arrest, season of arrest (spring, summer, autumn, or winter), time of arrest (daytime or nighttime), and region of arrest (north, east, west, or south). We performed 1:1 nearest-neighbor matching on the propensity score with a caliper of 0.2 without replacement between patients with and without bystander CPR.[25] We confirmed the success of the propensity matching procedure by comparing the baseline characteristics with standardized differences within $\pm$ 10%.[26] We reported risk ratios (RR) of neurologically favorable survival for patients with versus without bystander CPR with 95% confidence intervals (CIs).

### *Subgroup analysis*

Subgroup analysis was performed to further characterize the association between bystander CPR and favorable neurologic outcomes after OHCA due to drowning according to predefined subgroups: children ($<$18 y) or adults ($\geq$18 y). Difference among subgroups was assessed by including an interaction term between the treatment variable (bystander CPR vs. no CPR) and the subgroup variable of interest in the propensity score-matched cohort.

### *Sensitivity analysis*

Sensitivity analyses (i.e., propensity score adjustment model and multivariable regression models) were performed to verify that results of comparison between patients with and without bystander CPR did not depend on the method of covariate adjustment of the propensity score matching (eFigure in the Supplement). Propensity score adjustment model was adjusted for a treatment variable (bystander CPR vs. no CPR) and the propensity score as a continuous variable. Multivariable regression models were adjusted for several different sets of variables (Models 1–3) and were conducted by dividing the cohort into early ($\leq$10 min) and late ($>$10 min) response time groups

(Models 4 and 5). Model 1 was adjusted for the treatment variable and pre-treatment variables (i.e., the same variables used for the estimation of the propensity score). Model 2 was adjusted for the treatment variable and pre- and post-treatment variables (i.e., defibrillation by EMS personnel, intravenous catheter insertion, epinephrine administration, advanced airway management, response time, and transport time). Model 3 was adjusted for the treatment variable and specific variables (i.e., the variables with significant difference between patients with and without bystander CPR in the full cohort). In Models 4 and 5, included patients were limited to those who were treated by EMS personnel early (response time $\leq$ 10 min) and late (response time > 10 min), respectively. We reported odds ratios (ORs) with 95% CIs for those sensitivity analyses.

We used JMP Pro 14.0.0 software (SAS Institute Inc., Cary, NC, USA) to conduct statistical analyses. We considered a two-sided *P* value of 0.05 statistically significant for all hypothesis tests.

## Results

During the study period, we identified 12,139 eligible patients with OHCA due to drowning (Fig. 1). Of these, 5157 (42.5%) received bystander CPR, and 6982 (57.5%) did not. 4345 patients receiving bystander CPR were propensity-matched with 4345 patients not receiving bystander CPR.

Table 1 summarizes the baseline characteristics of the full cohort according to bystander CPR. In the full cohort, 6291 patients (51.8%) were male, and the median age was 79 years (IQR, 70–85 years). More than 75% of patients were elderly ($\geq$70 years), and more than 90% of patients were unwitnessed. The initial rhythm was most commonly asystole (approximately 90% of patients).

Table 2 summarizes the baseline characteristics of the propensity score-matched cohort according to bystander CPR. After propensity score matching, the baseline characteristics were well balanced on pre-treatment characteristics between the two groups. As for post-treatment characteristics, although there were some missing data on prehospital care by healthcare professionals, the frequency of prehospital ALS tended to be high in the bystander CPR group. In addition, response time was shorter in the bystander CPR group compared with the no CPR group.

Table 3 shows the primary and secondary outcomes of patients with OHCA due to drowning in the full and propensity score-matched cohort. Bystander CPR was associated with an increased chance of neurologically favorable survival (0.4% vs. 0.8%; RR, 2.19; 95%CI, 1.21–3.95; $P = 0.0076$), one-month survival (1.1% vs. 1.7%; RR, 1.55; 95%CI, 1.09–2.22; $P = 0.0150$), and prehospital ROSC (2.7% vs. 3.5%; RR, 1.30; 95%CI, 1.03–1.65; $P = 0.0296$) in the propensity score-matched cohort, as well as in the full cohort.

In the subgroup analysis (Fig. 2), bystander CPR was associated with one-month neurologically favorable survival in adults (0.3% vs. 0.5%; RR, 2.11; 95%CI, 1.03–4.31), whereas no significant association was observed in children (5.3% vs. 9.7%; RR, 1.82; 95%CI, 0.66–4.99). There was no significant interaction for age (*P* for Interaction = 0.8168).

In the sensitivity analyses (eFigure in the Supplement), similar to the primary analysis using propensity score matching, bystander CPR was associated with increased chance of one-month neurologically favorable survival across a variety of sensitivity analyses. In addition, despite the time to treatment by EMS personnel, the association of bystander CPR with neurologically favorable survival did not change.

## Discussion

### Principal findings

In this nationwide population-based observational study, we found a significantly positive association of bystander CPR with neurologically favorable survival after OHCA due to drowning not only in unadjusted analysis but also propensity score-matched analysis. This association was consistent across a variety of sensitivity analyses. Similar positive associations were observed for one-month survival and prehospital ROSC.

### Epidemiology and characteristics of drowning in Japan

In Japan, there is a traditional custom to sit and soak up to the shoulders or neck in hot-water tubs almost every day, and approximately two thirds of deaths from drowning are associated with bathing.[27–30] Compared with other countries, the number of drowning patients is larger (7,000–9,000 patients per year) and most of them (three quarters or more) are the elderly aged $\geq$ 65 years in Japan.[27,28] In addition, the drowning mortality rate for the elderly in Japan is the highest in the world.[27–30]

Unfortunately, the information on the site of occurrence of cardiac arrest (e.g., bath, pool, pond, river, or sea) could not be obtained from the All-Japan Utstein Registry data. However, in light of health statistics in Japan,[27,28] the many OHCA patients due to drowning in our study may have been related to bathing.[29–34]

Furthermore, hot-water drowning is considered to have different pathophysiology and mechanisms of cardiac arrest from cold-water drowning (e.g., soaking in hot-water tubs can trigger cardiovascular changes such as dehydration, hypotension, thrombosis, and arrhythmias, or pouring hot water over the head can trigger reflex epilepsy; on the other hand, cardiac arrest related to cold water drowning is likely to have a respiratory or asphyxial etiology).[31,35]

Thus, careful attention may be required to interpret the results of our study on OHCA due to drowning, as the study population might be markedly different from the common drowning population in other countries.

### Comparison with other studies

Past studies on bystander CPR and outcomes after OHCA due to drowning are scarce. To our knowledge, no RCTs have examined the effect of bystander CPR in OHCA due to drowning. Several observational studies indicated that bystander CPR might not be associated with an increased chance of favorable outcomes after OHCA due to drowning.[9–12]

In a Sweden study,[10] including 255 patients with OHCA due to drowning reported to the Swedish OHCA Registry between 1990 and 2005, although the point estimate for the treatment effect favored bystander CPR, the 95% CIs for the point estimate overlapped unity (adjusted OR for one-month survival, 1.34; 95%CI, 0.41–4.32). This study might be insufficiently powered and produced wide confidence intervals. In another Sweden study,[9] including 529 patients with OHCA due to drowning reported to the Swedish OHCA Registry between 1990 and 2012, the multivariable analysis of one-month survival was shown to be non-significant for bystander CPR, although a significant difference was shown in unadjusted analysis. This study might also be underpowered to detect significant differences in one-month survival.

**Table 1 – Baseline characteristics of the full cohort according to bystander CPR.**

| Characteristic | Full cohort | | |
|---|---|---|---|
| | Total n = 12,139 | No CPR n = 6982 | Bystander CPR n = 5157 |
| Baseline characteristics | | | |
| Age, y | | | |
| - Median (IQR) | 79 (70–85) | 79 (70–85) | 79 (70–85) |
| - Mean (SD) | 73.7 (18.8) | 74.7 (16.3) | 72.3 (21.7) |
| Sex | | | |
| 1) Male - No. (%) | 6291 (51.8) | 3793 (54.3) | 2498 (48.4) |
| 2) Female - No. (%) | 5848 (48.2) | 3189 (45.7) | 2659 (51.6) |
| Witness | | | |
| 1) No witness - No. (%) | 11,309 (93.2) | 6513 (93.3) | 4796 (93.0) |
| 2) By family member - No. (%) | 303 (2.5) | 185 (2.6) | 118 (2.3) |
| 3) By non-family member - No. (%) | 527 (4.3) | 284 (4.1) | 243 (4.7) |
| Dispatcher's instruction for CPR | | | |
| 1) Yes - No. (%) | 7561 (62.3) | 3463 (49.6) | 4098 (79.5) |
| 2) No - No. (%) | 4578 (37.7) | 3519 (50.4) | 1059 (20.5) |
| Initial rhythm | | | |
| - Shockable rhythm | | | |
| 1) VF - No. (%) | 286 (2.4) | 136 (2.0) | 150 (2.9) |
| 2) VT - No. (%) | 4 (0.0) | 2 (0.0) | 2 (0.0) |
| - Non-shockable rhythm | | | |
| 3) PEA - No. (%) | 562 (4.6) | 266 (3.8) | 296 (5.8) |
| 4) Asystole - No. (%) | 11,028 (90.9) | 6545 (93.7) | 4483 (86.9) |
| - Others | | | |
| 5) Others (e.g., Bradycardia) - No. (%) | 259 (2.1) | 33 (0.5) | 226 (4.4) |
| Year of arrest | | | |
| 1) 2013 - No. (%) | 2813 (23.2) | 1589 (22.7) | 1224 (23.7) |
| 2) 2014 - No. (%) | 3162 (26.0) | 1795 (25.7) | 1367 (26.5) |
| 3) 2015 - No. (%) | 3153 (26.0) | 1827 (26.2) | 1326 (25.7) |
| 4) 2016 - No. (%) | 3011 (24.8) | 1771 (25.4) | 1240 (24.1) |
| Season of arrest | | | |
| 1) Spring (March, April, May) - No. (%) | 3069 (25.3) | 1811 (26.0) | 1258 (24.4) |
| 2) Summer (June, July, August) - No. (%) | 1720 (14.2) | 935 (13.4) | 785 (15.2) |
| 3) Autmun (September, October, November) - No. (%) | 2223 (18.3) | 1322 (18.9) | 901 (17.5) |
| 4) Winter (December, January, February) - No. (%) | 5127 (42.2) | 2914 (41.7) | 2213 (42.9) |
| Time of arrest | | | |
| 1) Daytime (7:00–22:59) - No. (%) | 9933 (81.8) | 5619 (80.5) | 4314 (83.7) |
| 2) Nighttime (23:00–6:59) - No. (%) | 2206 (18.2) | 1363 (19.5) | 843 (16.3) |
| Region of arrest | | | |
| 1) North - No. (%) | 1022 (8.4) | 570 (8.1) | 452 (8.8) |
| 2) East - No. (%) | 7002 (57.7) | 4117 (59.0) | 2885 (55.9) |
| 3) West - No. (%) | 4035 (33.2) | 2260 (32.4) | 1775 (34.4) |
| 4) South (Okinawa, Amami) - No. (%) | 80 (0.7) | 35 (0.5) | 45 (0.9) |
| Prehospital care by healthcare professionals | | | |
| Prehospital life support | | | |
| 1) BLS only - No. (%) | 4521 / 11,376 (39.7) | 2739 / 6499 (42.1) | 1782 / 4877 (36.5) |
| 2) Any ALS - No. (%) | 6855 / 11,376 (60.3) | 3760 / 6499 (57.9) | 3095 / 4877 (63.5) |
| Defibrillation - No. (%) | 385 / 11,028 (3.5) | 204 / 6086 (3.4) | 181 / 4942 (3.7) |
| Intravenous catheter insertion - No. (%) | 3962 / 11,495 (34.5) | 2127 / 6466 (32.9) | 1835 / 5029 (36.5) |
| Epinephrine administration - No. (%) | 1655 / 11,264 (14.7) | 858 / 6259 (13.7) | 797 / 5005 (15.9) |
| Advanced airway management - No. (%) | 5051 / 10,937 (46.2) | 2769 / 6208 (44.6) | 2282 / 4729 (48.3) |
| Response time, min | | | |
| - Median (IQR) | 9 (7–11) | 9 (7–12) | 9 (7–11) |
| - Mean (SD) | 10.6 (7.1) | 11.3 (8.4) | 9.7 (4.8) |
| Transport time, min | | | |
| - Median (IQR) | 23 (18–30) | 24 (18–31) | 23 (18–30) |
| - Mean (SD) | 24.9 (9.6) | 25.0 (9.6) | 24.6 (9.6) |

The data are expressed as the number (%) of patients, the mean (SD), or the median (IQR), unless otherwise indicated.
Abbreviations: ALS, Advanced life support; BLS, Basic life support; CPR, Cardiopulmonary resuscitation; IQR, Interquartile range; SD, Standard deviation; PEA, Pulseless electrical activity; VF, ventricular fibrillation; VT, Ventricular tachycardia.

**Table 2 – Baseline characteristics of the propensity score-matched cohort according to bystander CPR.**

| Characteristic | Propensity score-matched cohort | | |
|---|---|---|---|
| | No CPR n = 4345 | Bystander CPR n = 4345 | Standardized Difference (%) |
| Baseline characteristics | | | |
| Age, y | | | |
| - Median (IQR) | 79 (71–85) | 80 (72–86) | NA |
| - Mean (SD) | 75.5 (16.2) | 75.4 (17.8) | 0.7045 |
| Sex | | | |
| 1) Male - No. (%) | 2240 (51.6) | 2157 (49.6) | 3.8210 |
| 2) Female - No. (%) | 2105 (48.4) | 2188 (50.4) | −3.8210 |
| Witness | | | |
| 1) No witness - No. (%) | 4115 (94.7) | 4106 (94.5) | 0.8853 |
| 2) By family member - No. (%) | 94 (2.2) | 92 (2.1) | 0.2764 |
| 3) By non-family member - No. (%) | 136 (3.1) | 147 (3.4) | −1.4088 |
| Dispatcher's instruction for CPR | | | |
| 1) Yes - No. (%) | 3357 (77.3) | 3357 (77.3) | 0.0000 |
| 2) No - No. (%) | 988 (22.7) | 988 (22.7) | 0.0000 |
| Initial rhythm | | | |
| - Shockable rhythm | | | |
| 1) VF - No. (%) | 87 (2.0) | 93 (2.1) | −0.9833 |
| 2) VT - No. (%) | 2 (0.0) | 1 (0.0) | 1.6039 |
| - Non-shockable rhythm | | | |
| 3) PEA - No. (%) | 187 (4.3) | 178 (4.1) | 0.9971 |
| 4) Asystole - No. (%) | 4036 (92.9) | 4038 (92.9) | −0.1558 |
| - Others | | | |
| 5) Others (e.g., Bradycardia) - No. (%) | 33 (0.8) | 35 (0.8) | −0.5666 |
| Year of arrest | | | |
| 1) 2013 - No. (%) | 980 (22.6) | 995 (22.9) | −0.8352 |
| 2) 2014 - No. (%) | 1118 (25.7) | 1131 (26.0) | −0.6850 |
| 3) 2015 - No. (%) | 1158 (26.6) | 1144 (26.3) | 0.7252 |
| 4) 2016 - No. (%) | 1089 (25.1) | 1075 (24.8) | 0.7400 |
| Season of arrest | | | |
| 1) Spring (March, April, May) - No. (%) | 1058 (24.4) | 1073 (24.7) | −0.8135 |
| 2) Summer (June, July, August) - No. (%) | 537 (12.4) | 535 (12.3) | 0.1521 |
| 3) Autmun (September, October, November) - No. (%) | 784 (18.0) | 800 (18.4) | −0.9584 |
| 4) Winter (December, January, February) - No. (%) | 1966 (45.2) | 1937 (44.6) | 1.3470 |
| Time of arrest | | | |
| 1) Daytime (7:00-22:59) - No. (%) | 3581 (82.4) | 3554 (81.8) | 1.6177 |
| 2) Nighttime (23:00-6:59) - No. (%) | 764 (17.6) | 791 (18.2) | −1.6177 |
| Region of arrest | | | |
| 1) North - No. (%) | 368 (8.5) | 380 (8.8) | −0.9982 |
| 2) East - No. (%) | 2515 (57.9) | 2503 (57.6) | 0.5466 |
| 3) West - No. (%) | 1440 (33.1) | 1444 (33.2) | −0.1911 |
| 4) South (Okinawa, Amami) - No. (%) | 22 (0.5) | 18 (0.4) | 1.4779 |
| Prehospital care by healthcare professionals | | | |
| Prehospital life support | | | |
| 1) BLS only - No. (%) | 1510 / 3984 (37.9) | 1467 / 4132 (35.5) | NA |
| 2) Any ALS - No. (%) | 2474 / 3984 (62.1) | 2665 / 4132 (64.5) | NA |
| Defibrillation - No. (%) | 109 / 3566 (3.1) | 131 / 4188 (3.1) | NA |
| Intravenous catheter insertion - No. (%) | 1425 / 3886 (36.7) | 1616 / 4264 (37.9) | NA |
| Epinephrine administration - No. (%) | 581 / 3691 (15.7) | 681 / 4239 (16.1) | NA |
| Advanced airway management - No. (%) | 1831 / 3749 (48.8) | 1980 / 4021 (49.2) | NA |
| Response time, min | | | |
| - Median (IQR) | 8 (7–11) | 9 (7–11) | NA |
| - Mean (SD) | 10.2 (6.8) | 9.7 (4.7) | NA |
| Transport time, min | | | |
| - Median (IQR) | 23 (18–30) | 23 (18–30) | NA |
| - Mean (SD) | 24.8 (9.5) | 24.7 (9.6) | NA |

The data are expressed as the number (%) of patients, the mean (SD), or the median (IQR), unless otherwise indicated.
Standardized differences within ± 10% were considered as inconsequential.
Abbreviations: ALS, Advanced life support; BLS, Basic life support; CPR, Cardiopulmonary resuscitation; IQR, Interquartile range; SD, Standard deviation; PEA, Pulseless electrical activity; VF, ventricular fibrillation; VT, Ventricular tachycardia.

**Table 3 – Outcomes of patients with versus without bystander CPR in the full and propensity score-matched cohort.**

| Outcome | Unadjusted Analysis | | | | Propensity Score-Matched Analysis | | | |
|---|---|---|---|---|---|---|---|---|
| | No CPR n = 6982 | Bystander CPR n = 5157 | RR (95%CI) | *P* value | No CPR n = 4345 | Bystander CPR n = 4345 | RR (95%CI) | *P* value |
| Favorable Neurologic outcome (CPC 1 or 2) - No. (%) | 23 (0.3) | 190 (3.7) | 11.18 (7.27–17.21) | <0.0001 | 16 (0.4) | 35 (0.8) | 2.19 (1.21–3.95) | 0.0076 |
| CPC 1 - No. (%) | 19 (0.3) | 174 (3.4) | NA | NA | 15 (0.4) | 30 (0.7) | NA | NA |
| CPC 2 - No. (%) | 4 (0.0) | 16 (0.3) | NA | NA | 1 (0.0) | 5 (0.1) | NA | NA |
| CPC 3 - No. (%) | 10 (0.2) | 17 (0.3) | NA | NA | 7 (0.2) | 9 (0.2) | NA | NA |
| CPC 4 - No. (%) | 37 (0.5) | 51 (1.0) | NA | NA | 22 (0.5) | 27 (0.6) | NA | NA |
| CPC 5 - No. (%) | 6903 (98.9) | 4894 (94.9) | NA | NA | 4296 (98.8) | 4269 (98.3) | NA | NA |
| CPC unknown - No. (%) | 9 (0.1) | 5 (0.1) | NA | NA | 4 (0.1) | 5 (0.1) | NA | NA |
| One-month survival - No. (%) | 79 (1.1) | 263 (5.1) | 4.51 (3.51–5.78) | <0.0001 | 49 (1.1) | 76 (1.7) | 1.55 (1.09–2.22) | 0.0150 |
| Prehospital ROSC - No. (%) | 152 (2.2) | 322 (6.2) | 2.87 (2.37–3.47) | <0.0001 | 116 (2.7) | 151 (3.5) | 1.30 (1.03–1.65) | 0.0296 |

The data are expressed as the number (%), unless otherwise indicated.
The association between bystander CPR and outcomes were reported as RRs with 95% CIs.
Abbreviations: CI, Confidence interval; CPC, Glasgow-Pittsburgh cerebral performance category; CPR, Cardiopulmonary resuscitation; RR, Risk ratio; ROSC, Return of spontaneous circulation.

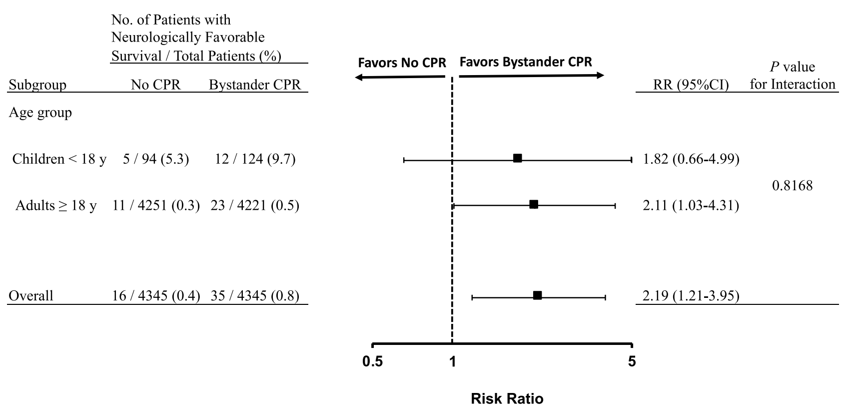


**Fig. 2 – Subgroup analyses for one-month neurologically favorable survival in the propensity score-matched cohort. The associations between bystander CPR and one-month neurologically favorable survival were reported as RRs with 95% CIs for predefined subgroup analysis according to age (children [<18 y] or adults [≥18 y]).**
**The *P* value represents the *P* value for the interaction between bystander CPR (yes or no) and a given subgroup.**
**Abbreviations: CI, Confidence interval; CPR, Cardiopulmonary resuscitation; RR, Risk ratio**

In a US study,[13] including 908 patients with OHCA due to drowning reported to the Cardiac Arrest Registry for Enhanced Survival (CARES) between 2013 and 2015, bystander CPR was associated with an increased chance of neurologically favorable survival (adjusted OR, 3.02; 95%CI, 1.85–4.92).[13] Our findings were consistent with the findings of that study, although the study populations were quite different between the two studies. The mean age of patients in the US study was 34.6 (SD, 26.0) years, whereas the mean age of patients in our study was 73.7 (SD, 18.8) years. Such difference in age between the two studies might be attributed to the cultural habit in Japan (i.e., Japanese-style bathing) or where the cardiac arrests occurred (e.g., bath, pool, pond, river, or sea).[29–33,35,36]

In pediatric studies,[11,12] although statistical adjustments might be difficult due to the small sample size, unadjusted analysis indicated that there was no difference in neurologically favorable survival between patients with and without bystander CPR. The result of our subgroup analysis in children was consistent with those studies. However, including our subgroup analysis in children (n = 218), the sample size might be too small to detect any difference in neurologically favorable survival both in the Netherlands study (n = 160)[11] and in the North America study (n = 30).[12] With a larger sample size, a statistically significant difference may have been shown even in children, as the point estimate for the treatment effect favored bystander CPR in children in our subgroup analysis, as is the case with adults.

In a previous Japan study,[37] including 68 children and 1669 adults with OHCA due to drowning reported to the Utstein Osaka Registry of OHCA between 1999 and 2010, children had significantly better outcomes compared with adults. Our findings also indicated that children might have a much greater chance of surviving with favorable neurological outcomes compared with adults in OHCA due to drowning (Fig. 2). In the future, a sufficiently powered study should be undertaken in pediatric patients with OHCA due to drowning.

### *Strengths and weaknesses of the study*

Our study had several strengths, by including the large sample size, using the government-led nationwide population-based registry data that routinely collected prehospital care data and outcome records for all OHCA patients including children in Japan, and performing the several robust covariate adjustment methods.

Our study had several limitations. First, this registry was not based on the Utstein reporting template for drowning, but on the Utstein reporting template for cardiac arrest. Therefore, we could not address several important data (e.g., water temperature, submersion duration, or body of water) recommended to collect in the Utstein reporting guidelines for drowning,[16] although these factors could affect the outcomes after OHCA due to drowning.[38,39] Second, despite efforts to control for selection bias and confounders using a variety of analytical techniques, the potential for unmeasured confounding and residual selection bias remain. Therefore, our findings may not necessarily derive causality but association. Third, the patient selection in our study could limit the generalizability because the characteristics of patients with OHCA due to drowning were slightly different between the included and excluded patients (eTable in the Supplement). In addition, the generalizability of our findings to other countries is uncertain. The characteristics of drowned patients (e.g., common age and site of occurrence) in Japan may differ from those in other countries. In Japan, drowned patients might be older and drowning might more frequently occur in the bath compared with other countries. Fourth, although the subgroup analysis by age ($<$18 or $\geq$18 years) was conducted in our study, the sample size of pediatric patients might be too small to detect a statistically significant difference. In addition, further subdivision might be necessary to reflect age-specific patient characteristics. An adequately powered study would be required to assess whether bystander CPR would be associated with an increased chance of neurologically favorable survival after pediatric OHCA due to drowning. Fifth, similar to other registry-based studies, the recorded etiologies of cardiac arrest in this registry were less well validated than those in planned prospective studies. Due to the anonymization of patient data, comparing the registry data with the medical record data at the patient level was impossible. Sixth, it was difficult to assess the quality of bystander CPR. In addition, it was unknown whether the recorded data on bystander CPR were based on visual confirmation by EMS personnel or interviews with bystanders. Although compression-only CPR is commonly used in Japanese citizens, compression-only CPR might be ineffective in several situations where the cardiac arrest could have the respiratory or asphyxial etiology. On the other hand, the answer of the question which type of bystander CPR is superior, conventional CPR (with rescue breathing) or compression-only CPR (without rescue breathing), for patients with OHCA due to drowning may vary depending on the drowning population (e.g., children vs adults, hot vs cold water, or cardia vs respiratory etiology). Thus, the type of bystander CPR could affect the outcomes after OHCA due to drowning. Further study collecting more detailed information on drowning (e.g., body of water, or actual etiology of arrest) would be required to determine which type of bystander CPR is more effective for OHCA due to drowning. In addition, the performance of dispatcher instruction was not necessarily synonymous with the implementation of bystander CPR by the bystander in this study. Although there may be several reasons for why the bystander did not follow the dispatcher instruction (e.g., physical distance, psychological resistance, or futility of resuscitative efforts) and the reactions by bystanders may influence outcomes after OHCA due to drowning, we could not assess what instruction was given by the dispatcher or why the bystander did not follow the dispatcher instruction. Seventh, the data on in-hospital or post-resuscitation care that could affect the outcomes after OHCA due to drowning were unavailable, although patients with OHCA are principally transported to a tertiary emergency medical center in each region and these centers have similar levels of capability. Finally, data on complications and longer-term outcomes were unavailable in this registry.

## Conclusions

The results of this nationwide population-based observational study of OHCA due to drowning from 2013 to 2016 indicated that bystander CPR was associated with increased chance of neurologically favorable survival. As is the case with OHCA due to primary cardiac cause, public awareness should be focused on the need for providing bystander CPR in OHCA due to drowning, although further studies are required to determine the effect of bystander CPR in children and to identify the optimal type of CPR.

## Author contributions

TF is the guarantor and takes responsibility for the integrity of the data and the accuracy of the data analysis.

TF conceived and designed the study. TF and IK acquired the data. TF, NO-F, KH, and IK contributed substantially to the analysis or interpretation of data. TF authored the initial and final drafts of the manuscript. All authors revised drafts of the manuscript.

All authors approved the final, submitted version of the manuscript.

## Other contributions

We thank the Fire and Disaster Management Agency who collected and managed the All-Japan Utstein Registry data.

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This study was supported by University of the Ryukyus. Funding sources had no role in the study design, analysis and interpretation of the data, and writing of the paper.

## Funding sources

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## Conflict of interest

None.

## Prior abstract Publication/Presentation

None.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:10.1016/j.resuscitation.2019.06.005.

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