Temporal Trends in Outcomes after Out-of-Hospital Cardiac Arrests Witnessed by Emergency Medical Services in Japan: A Population-Based Study

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TEMPORAL TRENDS IN OUTCOMES AFTER OUT-OF-HOSPITAL CARDIAC ARRESTS WITNESSED BY EMERGENCY MEDICAL SERVICES IN JAPAN: A POPULATION-BASED STUDY

Kentaro Kajino, MD, PhD, Tetsuhsita Kitamura, MD, MS, DPH, Kosuke Kiyohara, DPH, Taku Iwami, MD, MPH, PhD, Mohamud Daya, MD, MS, Marcus Eng Hock Ong, MBBS, MPH, Takeshi Shimazu, MD, Daikai Sadamitsu, MD

ABSTRACT

Objective: Survival after out-of-hospital cardiac arrests (OHCA) witnessed by emergency medical service (EMS) personnel has been insufficiently understood. The aim of this study was to evaluate temporal trends in survival after EMS-witnessed OHCA in Japan. Methods: A nationwide, population-based, observational cohort study of consecutive adult OHCA patients with emergency responder resuscitation attempts from January 2005 to December 2012 in Japan. We assessed the trends in annual incidence, characteristics, and outcomes of OHCA patients witnessed by EMS personnel. Multiple logistic regression analysis was used to assess factors that were potentially associated with neurologically favorable outcome defined as cerebral performance category 1 or 2. Results: During the study period, a total of 66,760 EMS-witnessed OHCA cases were documented. The annual incidence rates per 100,000 persons of EMS-witnessed OHCA patients increased from 4.6 (n = 7219) in 2005 to 4.9 (n = 9256) in 2012 (p for trend = 0.035). The proportion of one-month survival with neurologically favorable outcome improved from 5.9% in 2005 to 8.6% in 2012 (p for trend < 0.001), and the proportion increased from 22.1% in 2005 to 30.2% in 2012 in cases with shockable rhythm (p for trend < 0.001). In a multivariate analysis, adults, male gender, shockable rhythm, presumed cardiac origin, and year were associated with a better neurological outcome. Conclusions: In this population, the proportion of one-month survival with neurologically favorable outcome among OHCA patients witnessed by EMS personnel significantly improved during the study period. Key words: cardiac arrest; cardiopulmonary resuscitation; emergency medical services; outcome

INTRODUCTION

Sudden Cardiac arrest (SCA) is an important public health problem in advanced countries. More than 120,000 out-of-hospital cardiac arrest (OHCA) cases annually were transported to hospitals in Japan, and the numbers are increasing year by year. Recent improvements of the “chain of survival” in Japan has improved the survival outcome of OHCA cases, but it is still low overall compared to the best reported outcomes worldwide.

A lot of previous reports have been focused on the outcomes of OHCA witnessed by bystanders. For example, a population-based OHCA registry in Japan has been in existence since 2005. It reports that the proportion of OHCA cases witnessed by bystanders increased from 18.0% in 2005 to 21.5% in 2009, and the proportion of the neurologically favorable survivors improved from 2.1% in 2005 to 4.3% in 2009. In order to improve the outcomes of all OHCA cases, it is also crucial to evaluate the prehospital care quality and characteristics of OHCA cases witnessed by emergency medical service (EMS) personnel. However, there are few papers regarding EMS-witnessed OHCA cases, and the implications have been poorly understood.

In this study, we evaluated overall temporal incidence and outcomes of OHCA cases witnessed by EMS personnel by using a prospective, nationwide Utstein database of the Fire and Disaster Management Agency (FDMA) of Japan, covering eight years of data from...
January 1, 2005, to December 31, 2012. In addition, we assessed factors related to neurologically favorable survival after EMS-witnessed OHCAs using multivariate analysis.

**METHODS**

**Study Design and Setting**

Details of this registry have been previously described.® The All-Japan Registry by the FDMA is a nationwide, population-based registry of OHCAs that is based on the standardized Utstein style.6,7 This study enrolled all adults aged ≥ 20 years old with OHCA of cardiac and non-cardiac origins in whom resuscitation was attempted and was witnessed by EMS personnel, and who were then transported to medical institutions from January 1, 2005, through December 31, 2012. The ethics committee at Kyoto University and Osaka University Graduate School of Medicine approved the study.

Cardiac arrest was defined as the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation.5,6 The cardiac arrest was presumed to be of cardiac origin unless it was caused by cerebrovascular disease, respiratory disease, malignant tumors, external causes including trauma, hanging, drowning, drug overdose, and asphyxia, or any other non-cardiac cause. These diagnoses of cardiac or non-cardiac origin were clinically made by the physicians in charge in collaboration with EMS personnel.

**Emergency Medical Service Systems in Japan**

Japan has an area of 378,000 km², including both urban and rural communities, its population was 127 million inhabitants in 2014. EMS is provided by municipal governments via fire departments. There were 752 fire departments with dispatch centers, and approximately 5.9 million EMS dispatches were performed in 2014.2 The free emergency telephone number 1-1-9 is used to call for an ambulance from anywhere in Japan. Usually, a fire department ambulance has a crew of three emergency providers, including at least one emergency lifesaving technician (ELST). ELSTs are trained to insert an intravenous line, place adjunct airways, and use semi-automated external defibrillators for OHCA patients. Specially trained emergency life-saving technicians have been permitted to insert endotracheal tubes since July 2004 and to administer intravenous epinephrine since July 2006. Citizen use of an automated external defibrillator (AED) has been legally permitted since July 2004 in Japan. EMS providers are not permitted to terminate resuscitation in the field. Therefore, most patients with OHCA treated by EMS personnel were transported to a hospital and registered in this registry, excluding those with decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis. All EMS providers had been performing and teaching CPR according to the Japanese CPR guidelines.8–10 In Japan, about 1.6 million citizens participated in conventional CPR training programs consisting of chest compressions, mouth-to-mouth ventilation, and AED use offered mainly by local fire departments.2 The protocol for prehospital advanced treatments such as epinephrine administration, tracheal intubation, and intravenous fluid is basically uniform and strictly based on the ELST act.11

**Data Collection and Quality Control**

Data were collected with the use of a form based on the Utstein-style guidelines for reporting OHCA,6,7 and included details on gender, age, witness status, initial cardiac rhythm, time course of resuscitation, bystander-initiated CPR, endotracheal intubation, intravenous epinephrine, as well as prehospital return of spontaneous circulation (ROSC), one-month survival, and neurological status one month after the event. The time course of resuscitation included details on the time the call was received, time of contact with the patient and time of hospital arrival. All survivors were evaluated at one month after the event for their neurological function by the EMS personnel in charge via telephone follow up.

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 logic checks by the computer system and data were confirmed by the implementation working group. If a data form was incomplete, the FDMA would return it to the respective fire station for completion and follow up on the missing data.

**Outcome Measures**

Neurologic outcomes were 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.6,7 Our study endpoints were one-month survival and one-month survival with neurologically favorable outcome, defined as CPC category 1 or 2.4

**Statistical Analysis**

First, we assessed the temporal trends in annual incidence of OHCA patients witnessed by EMS personnel during the study period. The annual incidences
per 100,000 persons were calculated with the use of the estimated Japanese population data in each year.\(^\text{12}\) Second, temporal trends of patient and EMS characteristics and outcomes (return of spontaneous circulation [ROSC], one-month survival, and one-month survival with neurologically favorable outcome) were tested with univariate regression models for categorical variables and linear tests for numerical variables. Third, odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated to assess factors associated with one-month survival and one-month survival with neurologically favorable outcome using multivariate logistic regression models. Potential confounding factors that were biologically essential and considered to be associated with outcomes were included in the multivariate analysis. Those factors included age (adults aged 20–64 vs. elderly aged \(\geq 65\) years old), gender (men vs. women), etiology (cardiac vs. non-cardiac), shocks by EMS personnel (yes vs. no), intravenous fluid (yes vs. no), endotracheal intubation (yes vs. no), adrenaline administration (yes vs. no), and the time interval from call to contact with a patient by EMS (for one-minute increments), and year (for one-year increments). In addition, we assessed the trends in the proportions of neurologically favorable outcome by age group (adults or elderly), origin of arrest (cardiac or non-cardiac origins), and EMS shocks (yes or no) for a subgroup analysis. Their interaction p-values were also calculated.

All statistical analyses were performed using SPSS statistical package ver20.0J (SPSS, Inc., Chicago, IL). All of the tests were 2-tailed and a \(p\) value of \(<0.05\) was considered statistically significant.

**RESULTS**

A total of 925,288 OHCA cases were registered during these 8 years. Of them, 893,820 were adults with resuscitation attempts. Excluding 2305 victims without information on witness status (0.3%), 72,618 (8.1%) were witnessed by EMS personnel, 291,273 (32.6%) were witnessed by bystanders, and 527,624 (59.0%) were not witnessed. Among 72,618 EMS-witnessed OHCA cases, 66,760 were eligible for our analyses, excluding 5858 victims whose records of CPR or resuscitation time were missing or were obviously incorrect. The annual incidence rates per 100,000 persons of EMS-witnessed OHCA patients increased from 4.6 in 2005 to 4.9 in 2012 (\(p\) for trend \(=0.035\)) (Figure 1). Although the incidence among men remained stable (\(p\) for trend \(=0.190\)), the incidence among women increased from 2.8 in 2005 to 3.1 in 2012 (\(p\) for trend \(=0.008\)).

Table 1 shows temporal trends in characteristics and outcomes from OHCA cases witnessed by EMS personnel during the study period. The mean age increased from 70.6 years old in 2005 to 73.6 years old in 2012 (\(p\) for trend \(<0.001\)). The proportion of OHCA among men decreased from 62.9% in 2005 to 59.5% in 2012, but the proportion of shockable rhythms was stable (\(p\) for trend \(=0.107\)). As for prehospital advanced life supports, the proportion of adrenaline administration increased from 0.0% in 2005 to 11.5% in 2012, endotracheal intubation 1.7% to 3.8%, and fluid administration 5.5% to 22.4% (\(p\) for trend \(<0.001\)), respectively. The time from call to contact with patients by EMS lengthened from 8.0 mins in 2005 to 9.1 mins in 2012, and hospital arrival time also lengthened from 33 mins to 38 mins (\(p\) for trend \(<0.001\)). Temporal trends in outcomes for OHCA cases witnessed by EMS personnel are also noted in Table 1. The proportion of prehospital ROSC significantly increased from 12.6% in 2005 to 18.3% in 2012 (\(p\) for trend \(<0.001\)). The proportions of one-month survival (from 10.1% in 2005 to 13.7% in 2012, \(p\) for trend \(<0.001\)) and favorable neurological outcome (from 5.9% in 2005 to 8.6% in 2012, \(p\) for trend \(<0.001\)) significantly increased during the study period.
In a multivariate analysis, factors associated with one-month survival and one-month survival with favorable neurological outcome after EMS-witnessed OHCA are shown in Table 2. After adjusted prehospital confounding factors, adults (adjusted OR 1.78, 95% CI 1.67–1.90), male gender (adjusted OR 1.17, 95% CI 1.09–1.25), shockable rhythm (adjusted OR 6.41, 95% CI 5.99–6.85), presumed cardiac origin (adjusted OR 2.47, 95% CI 2.29–2.66), and year (adjusted OR for one-year increase 1.10, 95% CI 1.09–1.12) were associated with a better neurological outcome. On the other hands, intravascular fluid (adjusted OR 0.52, 95% CI 0.46–0.59), adrenaline administration (adjusted OR 0.42, 95% CI 0.33–0.53), endotracheal intubation (adjusted OR 0.34, 95% CI 0.26–0.46), and delayed EMS response time (adjusted OR for one-minute increase 0.98, 95% CI 0.98–0.99) were associated with a worse outcome. As for one-month survival, the adjusted ORs were similar to those for favorable neurologic outcome.

Subgroup analyses of temporal trends for favorable neurologic outcome from OHCA witnessed by EMS personnel are shown in Table 3. The proportion of favorable neurologic outcome increased from 8.7% in 2005 to 13.2% in 2012 among adults (p for trend < 0.001) and from 4.7% to 7.1% among elderly (p for trend < 0.001). The proportion increased from 22.1% in 2005 to 30.2% in 2012 in OHCA cases with shockable rhythm (p for trend < 0.001) and from 3.3% to 5.4% among those with nonshockable rhythm (p for trend < 0.001). There were no interactions between the 2 groups; age (adults and elderly), etiology (cardiac and non-cardiac), and rhythm (shockable and nonshockable).

**DISCUSSION**

From this large-scale OHCA registry in Japan, we demonstrated that the incidence of OHCA witnessed by EMS personnel slightly increased and the one-month survival with favorable neurological outcome significantly improved during the study period. In addition, related factors for neurologically favorable outcome were male gender, cardiac origin, and shockable rhythms. Although many previous reports described improved outcomes among OHCA cases witnessed by bystanders, the findings from this study focusing on epidemiology and outcomes of EMS-witnessed OHCA provides additional useful information. This has implications on the design, structure and quality of care of EMS systems in Japan and elsewhere.

A previous study from Sweden showed that the proportion of OHCA cases witnessed by EMS personnel doubled (from 8.5% to 16.9%) over 12 years from 1990–2009,13,14 but the annual incidence per 100,000 persons of OHCA in this study showed only a slight increment of EMS-witnessed OHCA incidence.
Reasons offered for the increasing proportion of EMS-witnessed OHCAs in Sweden were improvement of recognition both of OCHA by witnesses and their prodromal symptoms before OHCA by patients. However this explanation from the Swedish study might not hold true in Japan. Although early recognition and calling 119 may get EMS personnel to patients sooner, this explanation from the Swedish study might not hold true in Japan. Although early recognition and calling 119 may get EMS personnel to patients sooner, this explanation from the Swedish study might not hold true in Japan. Although early recognition and calling 119 may get EMS personnel to patients sooner, this explanation from the Swedish study might not hold true in Japan.

Comparison of the incidence and outcomes of OHCA in Japan, Sweden, and North America are shown in Table 4. Although the proportion of EMS-witnessed OHCAs during the 8-years in Japan was 8.1%, that proportion in Sweden and the Resuscitation Outcome Consortium (ROC) from North America were 13.5% and 10.2%, respectively. In addition, the proportion of EMS-witnessed OHCAs with shockable rhythm was only 13.3% in Japan whereas that of those with shockable rhythm was 51% in Sweden and 25% in the ROC study. About 50% of OHCAs witnessed by EMS personnel in Japan were of cardiac etiology but over two-thirds of EMS-witnessed OHCA patients in Sweden had a cardiac etiology, which might explain the differences in their proportion. Indeed, the annual incidence per 100,000 persons of cardiovascular-related deaths was 151.6 in Japan, 198 in North America, and 259.8 in Sweden, and the racial and regional variations in cardiovascular diseases including SCA would also affect their proportions and outcomes.

This study underscored that the temporal trends in outcomes from EMS-witnessed OHCAs were significantly improved in Japan irrespective of age group, cause of arrest, and rhythm. In the Swedish study, Axelsson and colleagues described that the definitive mechanisms regarding the improved OHCA survival witnessed after EMS arrival were unknown. However, one of the possible factors might be that these patients were treated more intensively after hospitalization.

### Table 2. Factors associated with outcomes from OHCAs witnessed by EMS personnel

<table>
<thead>
<tr>
<th></th>
<th>One-Month Survival</th>
<th>Neurologically Favorable Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude OR (95% CI)</td>
<td>Adjusted OR (95% CI)</td>
</tr>
<tr>
<td>Adults (versus elderly)</td>
<td>1.61 (1.53–1.69)</td>
<td>1.49 (1.41–1.56)</td>
</tr>
<tr>
<td>Men</td>
<td>1.18 (1.12–1.24)</td>
<td>1.01 (0.96–1.06)</td>
</tr>
<tr>
<td>Cardiac origin</td>
<td>1.94 (1.85–2.04)</td>
<td>1.58 (1.50–1.66)</td>
</tr>
<tr>
<td>Intravascular fluid</td>
<td>0.61 (0.57–0.66)</td>
<td>0.66 (0.61–0.73)</td>
</tr>
<tr>
<td>Intubation</td>
<td>0.26 (0.19–0.34)</td>
<td>0.24 (0.26–0.46)</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>0.99 (0.98–0.99)</td>
<td>0.98 (0.98–0.99)</td>
</tr>
<tr>
<td>EMS response time</td>
<td>1.05 (1.04–1.06)</td>
<td>1.08 (1.06–1.09)</td>
</tr>
</tbody>
</table>

### Table 3. Subgroup analyses of temporal trends in neurologically intact outcome from OHCAs witnessed by EMS personnel during the study period

<table>
<thead>
<tr>
<th></th>
<th>2005 n/N (%)</th>
<th>2006 n/N (%)</th>
<th>2007 n/N (%)</th>
<th>2008 n/N (%)</th>
<th>2009 n/N (%)</th>
<th>2010 n/N (%)</th>
<th>2011 n/N (%)</th>
<th>2012 n/N (%)</th>
<th>P for trend</th>
<th>Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>190/2172</td>
<td>192/2237</td>
<td>234/2135</td>
<td>250/2166</td>
<td>262/2261</td>
<td>295/2246</td>
<td>314/2140</td>
<td>299/2271</td>
<td>&lt;0.001</td>
<td>0.974</td>
</tr>
<tr>
<td>Elderly</td>
<td>238/5044</td>
<td>229/5389</td>
<td>301/5300</td>
<td>334/5858</td>
<td>379/6139</td>
<td>420/6971</td>
<td>476/6973</td>
<td>496/6970</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiac origin</td>
<td>343/3885</td>
<td>328/3957</td>
<td>408/3913</td>
<td>448/4399</td>
<td>505/4573</td>
<td>560/5156</td>
<td>639/5166</td>
<td>612/5035</td>
<td>&lt;0.001</td>
<td>0.745</td>
</tr>
<tr>
<td>Noncardiac origin</td>
<td>85/3331</td>
<td>93/3669</td>
<td>127/3522</td>
<td>136/3625</td>
<td>136/3847</td>
<td>155/4241</td>
<td>151/4217</td>
<td>183/4206</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Shockable</td>
<td>225/1016</td>
<td>217/996</td>
<td>278/980</td>
<td>279/1069</td>
<td>307/1139</td>
<td>344/1218</td>
<td>383/1225</td>
<td>362/1200</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Nonshockable</td>
<td>203/6200</td>
<td>204/6630</td>
<td>257/6455</td>
<td>305/6955</td>
<td>334/7281</td>
<td>371/8179</td>
<td>407/8158</td>
<td>433/8041</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

OHCA, out-of-hospital cardiac arrest; EMS, emergency medical service.
### Table 4. Comparisons of EMS-witnessed OHCAs in Japan, Sweden, and North America

<table>
<thead>
<tr>
<th></th>
<th>Japan</th>
<th>Sweden</th>
<th>North America</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of EMS-witnessed OHCAs among whole OHCA patients, n (%)</td>
<td>8.1</td>
<td>13.5</td>
<td>10.2</td>
</tr>
<tr>
<td>Proportion of patients with cardiac etiology among EMS-witnessed OHCA patients, n (%)</td>
<td>54.1</td>
<td>68.0</td>
<td>—</td>
</tr>
<tr>
<td>Proportion of shocked patients among EMS-witnessed OHCA patients, n (%)</td>
<td>13.3</td>
<td>51.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Outcomes among EMS-witnessed OHCA patients, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prehospital ROSC</td>
<td>15.1</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>ROSC</td>
<td>—</td>
<td>—</td>
<td>59.0</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>—</td>
<td>31.0</td>
<td>—</td>
</tr>
<tr>
<td>One month survival</td>
<td>12.1</td>
<td>16.0</td>
<td>—</td>
</tr>
<tr>
<td>Survival to hospital discharge</td>
<td>—</td>
<td>—</td>
<td>18.0</td>
</tr>
<tr>
<td>CPC 1 or 2</td>
<td>7.4</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

OHCA, out-of-hospital cardiac arrest; EMS, emergency medical service; ROSC, return of spontaneous resuscitation; CPC, cerebral performance category.

admission and the rescue team provided high-quality CPR before and after hospital arrival. A previous report in Japan also demonstrated that improvement of the CPR quality in prehospital settings or treatments after hospital arrival, might have influenced better outcomes after OHCA during the study period. In addition, a previous study demonstrated that area-based measurements and assessments led to improving outcomes from OHCA, and the registry itself might be contributing to the improved survival in Japan. However, further evaluation both of the prehospital CPR quality and post-resuscitation treatment is difficult, given that this data is not available in the Japan Utstein registry.

Furthermore, the proportion of one-month survival after OHCA witnessed by EMS personnel in Japan (increased from 10.1% in 2005 to 13.7% in 2012) was only 50% of that in Sweden (increased from 13.9% in 1992 to 21.8% in 2009). As there are differences in characteristics of race, population density, and health care systems between countries, it would be difficult to compare these outcomes. It is especially important whether termination of resuscitation (TOR) rules were performed in the field or not, as this will impact the survival denominator. On the other hand, the proportion of advanced life support (ALS) treatment delivered by EMS personnel such as epinephrine administration, intravenous fluid, and endotracheal intubation also increased during the study period. ALS procedures did not appear to contribute to improving outcomes. However, it would be difficult to assess the effect of ALS measures in this observational study because EMS personnel in Japan provide ALS procedures only for OHCA patients who do not respond to basic life support, resulting in some treatment bias. Some studies suggest that earlier epinephrine administration and earlier endotracheal intubation also contribute to improving outcomes after OHCA. Although this study did not show the positive association between ALS procedures and the outcomes from EMS-witnessed OHCA, this improvement in survival that occurred during the study period could be also explained partially by the changes to the CPR guidelines including the CPR quality. Prehospital treatments as well as special treatments after hospital arrival, such as target temperature management, might result in improved survival after OHCA. However, considering that the proportion of OHCA outcomes was lower in Japan than in other countries, further monitoring and efforts to improve outcomes after OHCA irrespective of witness status are needed.

This study has some inherent limitations. First, detailed data about the CPR quality by EMS personnel (e.g., compression rate, compression depth, CPR fraction, peri-shock pauses, and ventilation rate) were not available for our analyses. Second, our data does not address the potential impact of post-resuscitation care after hospital arrival such as hemodynamic support, induced hypothermia, and coronary intervention therapies. Third, the location of cardiac arrest such as home, public place, and nursing home was one of important factors associated with the outcome from OHCA, but All-Japan Utstein registry did not obtain information on location data. Therefore, we could not incorporate the location of cardiac arrest into multivariable models. Fourth, this was not a randomized controlled trial and although we adjusted for Utstein confounding variables in the multivariate analysis, other unknown confounding factors might exist that may have affected our findings.
CONCLUSION

This registry showed that the proportion of one-month survival with neurologically favorable outcome among OHCA patients witnessed by EMS personnel significantly improved during the study period in Japan. This might suggest that the quality of resuscitation provided by EMS and post-resuscitation care in Japan has improved over time.

References


