

## Continuous Improvements in “Chain of Survival” Increased Survival After Out-of-Hospital Cardiac Arrests A Large-Scale Population-Based Study

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**Background**—The impact of ongoing efforts to improve the “chain of survival” for out-of-hospital cardiac arrest (OHCA) is unclear. The objective of this study was to evaluate the incremental effect of changes in prehospital emergency care on survival after OHCA.

**Methods and Results**—This prospective, population-based observational study involved consecutive patients with OHCA from May 1998 through December 2006. The primary outcome measure was 1-month survival with favorable neurological outcome. Multiple logistic regression analysis was used to assess factors that were potentially associated with better neurological outcome. Among 42 873 resuscitation-attempted adult OHCA, 8782 bystander-witnessed arrests of presumed cardiac origin were analyzed. The median time interval from collapse to call for medical help, first cardiopulmonary resuscitation, and first shock shortened from 4 (interquartile range [IQR] 2 to 11) to 2 (IQR 1 to 5) minutes, from 9 (IQR 5 to 13) to 7 (IQR 3 to 11) minutes, and from 19 (IQR 13 to 22) to 9 (IQR 7 to 12) minutes, respectively. Neurologically intact 1-month survival after witnessed ventricular fibrillation increased from 6% (6/96) to 16% (49/297;  $P < 0.001$ ). Among all witnessed OHCA, earlier cardiopulmonary resuscitation (odds ratio per minute 0.89, 95% confidence interval 0.85 to 0.93) and earlier intubation (odds ratio per minute 0.96, 95% confidence interval 0.94 to 0.99) were associated with better neurological outcome. For ventricular fibrillation, only earlier shock was associated with better outcome (odds ratio 0.84, 95% confidence interval 0.80 to 0.88).

**Conclusions**—Data from a large, population-based cohort demonstrate a continuous increase in OHCA survival with improvement in the chain of survival. The incremental benefit of early advanced care on OHCA survival is also suggested. (*Circulation*. 2009;119:728-734.)

**Key Words:** cardiopulmonary resuscitation ■ heart arrest ■ death, sudden ■ epidemiology ■ ventricular fibrillation

Sudden cardiac arrest is a leading cause of adult death and has been an important public health problem in the industrialized world.<sup>1</sup> Approximately three fourths of deaths due to coronary heart disease occur in the out-of-hospital setting.<sup>2,3</sup> Extrapolation of the mortality rate observed in a recent large, prospective, multicenter observational study to the total population of the United States suggests that ≈300 000 people die annually in out-of-hospital settings in the United States.<sup>4</sup> During the last 3 decades, despite efforts to the contrary, survival after out-of-hospital cardiac arrests (OHCA) has not improved,<sup>5,6</sup> in contrast to the decline in

morbidity and mortality observed for most cardiovascular diseases.<sup>7-9</sup>

### Clinical Perspective p 734

The importance of using a “chain of survival” with early activation of emergency medical services (EMS), early cardiopulmonary resuscitation (CPR), early defibrillation, and early advanced life support (ALS) measures to decrease death and disability from OHCA has been accepted widely.<sup>1,10</sup> The benefit of early CPR and early defibrillation on survival has been shown in multiple settings<sup>5,11-14</sup>; however, overall sur-

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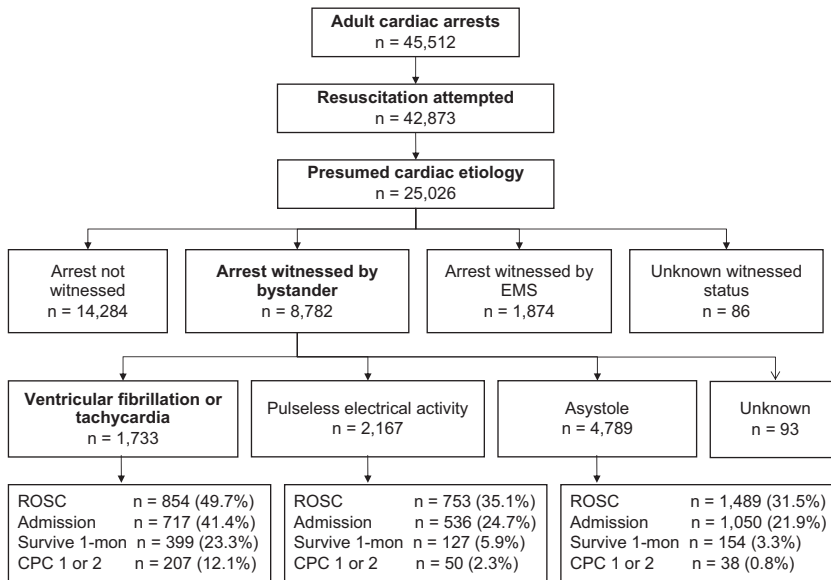
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**Figure 1.** Overview of EMS-treated cardiac arrests with an abridged Utstein template (May 1, 1998, to December 31, 2006). ROSC indicates return of spontaneous circulation; CPC, cerebral performance category; and mon, month.

vival after OHCA does not exceed 5% in most communities and is <3% in large urban populations.<sup>15-17</sup> The incremental benefit of ALS for OHCA remains to be determined.<sup>18-21</sup>

The Utstein Osaka Project, begun in 1998, is an ongoing large, prospective, population-based cohort study of OHCA in Osaka, Japan, that covers 8.8 million people.<sup>22-24</sup> More than 45 000 adult OHCA occurred from May 1998 through December 2006 in Osaka. During this period, some changes were made in the EMS system in this area to improve the chain of survival, such as training citizens in CPR and enabling EMS personnel to deliver shocks without online medical direction by physicians and to intubate in the field. The objectives of the present study were to determine whether improvement in the chain of survival increased survival after OHCA in a large population and to assess the incremental benefit of implementation of prehospital ALS programs on survival.

### Methods

#### Study Design, Population, and Setting

The investigation was a prospective, population-based cohort study of all persons 18 years or older with OHCA of presumed cardiac origin that was witnessed by bystanders and treated by EMS in Osaka Prefecture, Japan, from May 1, 1998, through December 31, 2006. The research protocol was approved by the institutional review board of Osaka University, with the assent of the EMS authorities and local governments in Osaka Prefecture.

Cardiac arrest was defined as the cessation of cardiac mechanical activities, as confirmed by the absence of signs of circulation.<sup>25</sup> The arrest was presumed to be of cardiac origin unless it was caused by trauma, drowning, drug overdose, asphyxia, exsanguination, or any other noncardiac causes determined by a physician in charge, in collaboration with the EMS rescuers.

#### EMS System in Osaka

Osaka Prefecture has approximately 8.8 million residents in an area of 1892 km<sup>2</sup>, which includes both urban and rural communities. The population is served by 35 fire stations, with a corresponding number of emergency dispatch centers. The EMS system is operated by the local fire stations, and life support is provided 24 hours per day via a single-tiered system in 33 stations and a 2-tiered system in 2 stations. The latter uses medics followed by physicians responding

by vehicle. The most highly trained prehospital emergency care providers are the Emergency Life-Saving Technicians (ELSTs). Each ambulance has 3 providers, and most have at least 1 ELST. The ELST system was started in 1991, but before 2003, they were allowed only to insert an intravenous line and an adjunct airway and to use a semiautomated external defibrillator for OHCA patients under the online medical direction of a physician. ELSTs have been allowed to deliver shocks without online medical direction since April 2003, and trained ELSTs have been allowed to insert tracheal tubes since July 2004 (tracheal intubation phase) and to use epinephrine since April 2006. Public access defibrillation programs were started in July 2004. CPR training for lay rescuers has been offered by local fire departments, the Japan Red Cross, Inc, and the Osaka Life Support Association throughout the study period. Approximately 120 000 citizens per year participate in conventional CPR training. No programs were in place to train individuals in compression-only CPR during this study period. Dispatcher instruction in CPR was introduced in July 1999.

#### Data Collection

Data were collected prospectively with a data form that included all core data recommended in the Utstein-style reporting guidelines for cardiac arrests,<sup>25</sup> such as sex, age, initial cardiac rhythm, time course of resuscitation, type of bystander-initiated CPR, return of spontaneous circulation, hospital admission, 1-month survival, and neurological status 1 month after the event. Special emphasis was placed on determining the time course of resuscitation. The time of EMS call receipt and time of vehicle arrival at the scene were recorded automatically at the dispatch center. The times of collapse and initiation of bystander CPR were obtained by EMS interview with the bystander before leaving the scene. The time of defibrillation was recorded by the semiautomated defibrillator. Watches of EMS personnel were synchronized with the clock at their dispatch center. During this study period, no change was made in this reporting system. Time interval from collapse to CPR was defined as the shorter of the time from collapse to CPR by bystanders and that by EMS personnel. The time interval from collapse to shock was defined as the shorter of the time from collapse to shock by bystanders and that by EMS personnel. The time interval from collapse to intubation was replaced with time to hospital arrival unless EMS personnel inserted an endotracheal tube in the field.

All survivors were followed up for up to 1 month after the event by EMS personnel. Neurological outcome was determined by a telephone interview 1 month after successful resuscitation that used the Cerebral Performance Category scale: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3,

severe cerebral disability; category 4, coma or vegetative state; and category 5, death.<sup>25</sup>

The methods of data collection and verification have been described previously.<sup>24</sup> Although a computer-based registration system was introduced in January 2005, the essentials of data collection were unaltered. Before the present study, a 6-month run-in period was used to ensure the completeness of episode identification and data capture. The steering committee of the present study verified uniform data collection, consistent definition of technical terms, and time synchronization to minimize these potential information biases. Because termination of resuscitation efforts and declaration of death are the exclusive domain of medical doctors in Japan, the only arrests that may have been missed from these data would be those associated with illegal activities that were not reported.

### Statistical Analysis

Analyses were conducted for both all EMS-treated, bystander-witnessed cardiac arrests of presumed cardiac origin and witnessed ventricular fibrillation (VF) cardiac arrests. The primary outcome measure was neurologically intact 1-month survival, defined as Cerebral Performance Category categories 1 or 2.<sup>25</sup> Secondary outcome measures included return of spontaneous circulation, admission to hospital, and 1-month survival.

Patient characteristics were evaluated with ANOVA for numerical variables and  $\chi^2$  test for categorical variables. Time trends in categorical values and numerical values were tested with univariable regression models and linear tests for trend, respectively. Multiple logistic regression analysis assessed the factors associated with better neurological outcome; odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. Potential confounding factors that were biologically essential or significantly associated with survival at  $P < 0.1$  in the univariable analyses were considered in the multivariable analyses. Both bystander-initiated, compression-only CPR and conventional CPR with rescue breathing were considered as bystander CPR, whereas bystander-initiated rescue breathing without compressions was classified as no bystander CPR. Interactions between bystander CPR and time to CPR and between tracheal intubation phase and time to tracheal intubation were also incorporated in multivariable analyses. Statistical analyses were performed with SPSS statistical package version 12.0J (SPSS, Inc, Chicago, Ill). A 2-sided  $P$  value of 0.05 or less was regarded as statistically significant.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

A total of 45 512 adult OHCA were documented during the 8 years and 8 months of the study period. Resuscitation was attempted in 42 873, and 25 026 OHCA were presumed to be of cardiac origin. Of these OHCA with presumed cardiac origin, 8782 were witnessed. Among them, 1733 (20%) had VF (including pulseless ventricular tachycardia), 2167 (25%) had pulseless electrical activity, and 4789 (55%) had asystole as the initial rhythm. We could not obtain data on the initial rhythm for 93 cases. Figure 1 provides an overview of the arrests, with the important outcomes by initial rhythms. The proportion of neurologically intact 1-month survival among those with witnessed VF, pulseless electrical activity, and asystole was 12%, 2%, and 1%, respectively.

Demographic and resuscitation characteristics of patients with witnessed cardiac arrest of presumed cardiac origin and witnessed VF arrests are noted in Table 1. Factors associated with 1-month survival with favorable neurological outcome included sex, age, location of arrest, activities of daily living status before arrest, VF as initial rhythm,

**Table 1. Patient Characteristics Throughout Study Period**

	Witnessed Cardiac Arrests of Presumed Cardiac Origin (n=8782)	Witnessed VF Cardiac Arrests (n=1733)
Age, y, mean (SD)	70.5 (15.2)	63.0 (14.2)
Male, n (%)	5546 (63.3)	1349 (78.0)
Location of arrests, n (%)		
Home	6014 (68.5)	900 (51.9)
Public space	1273 (14.5)	485 (28.0)
Work place	321 (3.7)	142 (8.2)
Healthcare facility*	695 (7.9)	62 (3.6)
Other	452 (5.1)	136 (7.8)
Activity of daily living before arrests, n (%)		
Good	6220 (70.8)	1481 (85.5)
Disability	2087 (23.8)	143 (8.3)
VF as initial rhythm, n (%)	1733 (19.9)	...
Bystander-initiated CPR, n (%)		
Compression-only CPR	1145 (13.1)	278 (16.1)
Conventional CPR	1565 (17.9)	348 (20.1)
Collapse to call, min		
Mean (SD)	4.9 (6.9)	3.0 (3.9)
Median (IQR)	3 (1–6)	2 (1–4)
Collapse to first CPR, min		
Mean (SD)	8.5 (7.0)	6.4 (5.2)
Median (IQR)	7 (3–12)	6 (2–9)
Collapse to first shock, min		
Mean (SD)	...	12.9 (6.2)
Median (IQR)	...	12 (9–16)
Collapse to intubation†, min		
Mean (SD)	26.9 (9.6)	26.2 (8.9)
Median (IQR)	26 (20–33)	26 (20–32)

\*Includes chronic care facilities and medical clinics.

†Time to tracheal intubation by EMS personnel in the field or hospital arrival.

bystander-initiated CPR, and time interval from collapse to the initiation of CPR by bystanders or EMS personnel. Time interval from collapse to intubation was included in the final model because it confounded the effect estimate for location of arrest.

Table 2 shows temporal trends in patient and EMS characteristics for bystander-witnessed cardiac arrests of presumed cardiac origin. The mean age of patients gradually increased from 68 to 72 years during the period ( $P$  for trend  $< 0.001$ ). The male/female ratio approximated 5:3 and showed no significant temporal trend ( $P$  for trend = 0.53). The proportion of those with VF as the initial rhythm increased from 16% to 25% ( $P$  for trend  $< 0.001$ ). The proportion of those who received bystander-initiated CPR also increased,

**Table 2. Patient and EMS Characteristics for Witnessed Cardiac Arrests of Presumed Cardiac Origin According to Time Period**

	1998 (n=598)	1999 (n=964)	2000 (n=987)	2001 (n=1035)	2002 (n=939)	2003 (n=1003)	2004 (n=975)	2005 (n=1083)	2006 (n=1198)
Age, y, mean (SD)	68.2 (16.0)	68.3 (15.4)	69.4 (15.7)	70.7 (14.8)	70.3 (14.5)	70.4 (15.5)	72.0 (14.8)	71.6 (15.2)	72.2 (14.5)
Male, n (%)	387 (65.0)	607 (63.4)	624 (63.4)	669 (65.0)	580 (61.9)	634 (63.3)	589 (60.4)	685 (63.3)	771 (64.4)
VF, n (%)	98 (16.4)	168 (17.4)	147 (15.1)	171 (16.8)	179 (19.3)	206 (20.7)	226 (23.3)	241 (22.3)	297 (24.8)
Bystander-initiated CPR, n (%)									
Compression-only CPR	44 (7.4)	112 (11.7)	96 (9.8)	133 (13.0)	117 (12.6)	136 (13.6)	152 (15.8)	156 (14.4)	199 (16.6)
Conventional CPR	68 (11.4)	127 (13.2)	148 (15.1)	182 (17.7)	181 (19.5)	196 (19.7)	203 (21.1)	227 (21.0)	233 (19.4)
Resuscitation time course, min, median (IQR)									
Collapse to call	4 (2–11)	4 (1–11)	4 (1–10)	3 (1–6)	3 (1–5)	3 (1–5)	3 (1–5)	3 (1–6)	2 (1–5)
Collapse to first CPR	9 (5–13)	8 (3–12)	8 (4–12)	8 (3–11)	7 (3–11)	7 (2–11)	7 (2–11)	7 (3–11)	7 (3–11)
Collapse to first shock*	19 (13–22)	17 (13–20)	14 (11–18)	14 (11–18)	14 (11–18)	11 (8–15)	11 (8–14)	10 (7–12)	9 (7–12)
Collapse to intubation†	25 (20–33)	25 (20–32)	26 (20–33)	26 (20–33)	26 (20–31)	27 (22–33)	28 (22–33)	26 (20–33)	25 (19–32)

\*Calculated for cases with VF as initial rhythm.

†Time to tracheal intubation by EMS personnel in the field or hospital arrival.

from 19% to 36% ( $P$  for trend  $<0.001$ ). Compression-only CPR accounted for  $>40\%$  of bystander-initiated CPR.

The median time interval from collapse to call for medical help shortened from 4 (interquartile range [IQR] 2 to 11) to 2 (IQR 1 to 5) minutes ( $P$  for trend=0.02). The median time interval from collapse to initiation of CPR decreased from 9 (IQR 5 to 13) to 7 (IQR 3 to 11) minutes ( $P$  for trend  $<0.001$ ) as the proportion of bystander-initiated CPR increased, whereas the time to CPR by EMS personnel remained  $\approx 7$  minutes (data not shown). The median time interval from collapse to first shock decreased significantly from 19 (IQR 13 to 22) to 9 (IQR 7 to 12) minutes ( $P$  for trend  $<0.001$ ) owing to the improvement in EMS response. Only 24 patients received shocks by bystanders during the study period. The median time to intubation remained around 25 minutes, but it took only 15 minutes ( $n=353$ ; IQR 12 to 20 minutes) when the specially trained ELST performed intubation in the field during the tracheal intubation phase. Thirteen percent (356/

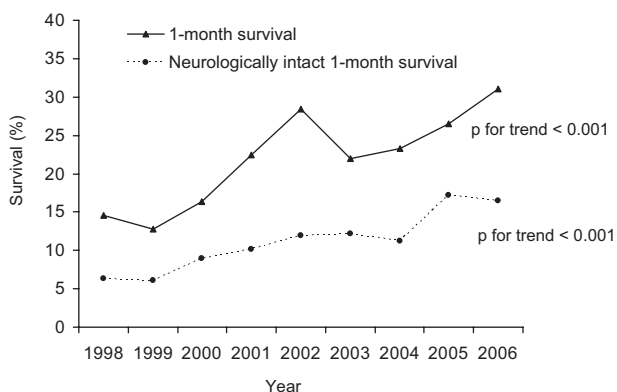
2745) of OHCA patients received intubation by specially trained ELSTs during the tracheal intubation phase.

One-month survival after all rhythms of witnessed cardiac arrests of presumed cardiac origin increased from 5% (31/591) to 12% (146/1197;  $P$  for trend  $<0.001$ ), and neurologically intact survival increased from 2% (12/591) to 6% (71/1197;  $P$  for trend  $<0.001$ ). One-month survival after witnessed VF cardiac arrests significantly increased from 15% (14/96) to 31% (92/297;  $P$  for trend  $<0.001$ ), and the proportion of neurologically intact 1-month survival also increased, from 6% (6/96) to 16% (49/297) during the period ( $P$  for trend  $<0.001$ ; Figure 2).

Table 3 shows the adjusted ORs and their 95% CIs for neurologically intact survival. Among all witnessed cardiac arrests of presumed cardiac origin, VF as the initial rhythm (OR 6.46, 95% CI 4.86 to 8.59), shorter time to CPR (OR for a 1-minute increase 0.89, 95% CI 0.85 to 0.93), and shorter time to intubation (OR for a 1-minute increase 0.96, 95% CI 0.94 to 0.99) were associated with better neurological outcome. With regard to witnessed VF cardiac arrests, only earlier shock was associated with a better outcome (OR for a 1-minute increase 0.84, 95% CI 0.80 to 0.88), whereas other resuscitation procedures were not.

## Discussion

This study showed that improvements in the chain of survival for OHCA were associated with increased survival in a large population. The time from collapse to CPR shortened from a median of 9 to 7 minutes because of the increase in bystander-initiated CPR, time to shock shortened from 19 to 9 minutes because of the refinement of the EMS system, and neurologically intact 1-month survival after witnessed VF cardiac arrests increased from 6% to 17% during the 8-year study period. To improve outcomes from OHCA, measures are



**Figure 2.** Temporal trend in survival after witnessed VF cardiac arrests.

**Table 3. Adjusted OR (95% CI) of Patient and EMS Characteristics for Neurologically Intact Survival After Witnessed Cardiac Arrests of Presumed Cardiac Origin and Witnessed VF Cardiac Arrests**

	Witnessed Cardiac Arrests of Presumed Cardiac Origin (n=8782)	Witnessed VF Cardiac Arrests (n=1733)
Female	1.51 (1.13–2.02)	1.52 (1.01–2.28)
Age $\geq$ 75 y	0.43 (0.30–0.61)	0.65 (0.40–1.05)
Location of arrests		
Home	Reference	Reference
Public space	1.33 (0.97–1.83)	1.13 (0.76–1.67)
Work place	1.75 (1.11–2.76)	1.90 (1.09–3.30)
Healthcare facility*	1.76 (1.00–3.08)	2.47 (1.09–5.60)
Other	0.91 (0.52–1.61)	0.91 (0.45–1.83)
Disability in activity of daily living before arrests	0.37 (0.21–0.62)	0.47 (0.20–1.08)
VF as initial rhythm	6.46 (4.86–8.59)	...
Bystander-initiated CPR	0.61 (0.39–0.94)	1.51 (0.88–2.61)
Collapse to first CPR†	0.89 (0.85–0.93)	1.00 (0.95–1.06)
Bystander CPR interaction	1.09 (1.01–1.17)	1.06 (0.95–1.17)
Collapse to shock by EMS†	...	0.84 (0.80–0.88)
Tracheal intubation phase	0.80 (0.37–1.72)	0.46 (0.17–1.26)
Collapse to tracheal intubation (ALS)†	0.96 (0.94–0.99)	0.97 (0.94–1.00)
Tracheal intubation interaction	1.03 (1.00–1.06)	1.03 (0.99–1.07)
Epinephrine by EMS	0.71 (0.25–2.05)	0.23 (0.03–1.78)

\*Includes chronic care facilities and medical clinics.

†OR for 1-minute increase in time.

needed to strengthen the chain of survival. Although uniform reporting of OHCA has been strongly recommended,<sup>1,25</sup> there have been only a few reports that continuously evaluated local EMS and resuscitation outcomes.<sup>5,6,13,21</sup> The present data, based on a large-scale, population-based cohort, provide further evidence of the effect of strengthening the chain of survival to save OHCA victims.

During the study period, some new measures were introduced. In April 2003, EMS personnel began to be allowed to deliver shocks without online medical direction, and the time interval from collapse to shock decreased by 3 minutes; however, survival did not improve similarly. Although dispatcher instruction in CPR was introduced in July 1999, no stepwise changes occurred in bystanders' behaviors and patient outcomes. The most plausible explanation for the observed improvement in survival is the accumulation of citizens trained in CPR in the population and continuous efforts of the EMS system.

The present study suggests the incremental benefit of some ALS procedures on survival after OHCA. Despite the broad use of advanced treatments for OHCA victims, evidence for the effectiveness of ALS treatment for OHCA is scarce.<sup>18</sup>

Several small, nonexperimental studies showed the effectiveness of ALS treatment,<sup>26–28</sup> whereas 2 meta-analyses showed no benefit of ALS for OHCA.<sup>19,20</sup> The Ontario Prehospital Advanced Life Support (OPALS) study, a large “before-and-after” controlled study of the effects of prehospital care, could not demonstrate a benefit of ALS treatments for OHCA.<sup>21</sup> However, the OPALS study adjusted for ALS phase (ie, before and after ALS program introduction) but not for the timing of field interventions, whereas we considered the time to intubation and showed the benefit of earlier advanced treatment. Both the type and timing of field ALS treatments might be important to increase survival after OHCA.

Although both the Utstein Osaka project and the OPALS study were large-scale, population-based cohort studies of OHCA, some differences were identified in clinical conditions. The proportion of patients who received bystander-initiated CPR increased to 36% at the end of the study period in Osaka, whereas the increase in the OPALS study was only 15%. The ALS program was added to the existing program of rapid defibrillation in the OPALS study, in which >90% victims received shocks within 8 minutes after call receipt, whereas only 36% in the present study received shocks within 8 minutes of call receipt. These differences may explain the discrepancy in the results, because early CPR initiated by bystanders and early defibrillation are critical factors for survival.<sup>1,10,29</sup> Furthermore, only specially trained ELSTs in Osaka are allowed to use ALS treatments, which resulted in only 13% of OHCA patients receiving intubation by them even during the tracheal intubation phase. The training and experience of EMS providers who perform ALS might also be different between the 2 study areas and affect the outcomes of OHCA.<sup>30</sup>

The increased survival in Osaka over time is due mainly to improvements in the first 3 links in the chain of survival. Although the present study suggests the benefit of early-initiated advanced cardiac care, we need to recognize that our data confirm the greater importance of early CPR and early shock for increasing survival after OHCA. ORs of time to CPR and time to shock for a 1-minute increase were less than that of time to intubation (ALS). These data are consistent with many previous studies that showed the importance of early CPR and shocks.<sup>21,29,31</sup> Emphasis should be placed on increasing bystander-initiated CPR and integrating such changes with improvements in ALS to save more lives.

The present study demonstrated continuous improvement in the chain of survival and OHCA survival, but absolute survival is still less than optimal. Although the proportion of those with bystander-initiated CPR increased in Osaka, approximately two thirds of OHCA victims still do not receive bystander-initiated CPR, and lay use of defibrillators has not been implemented widely. Bystander CPR is typically provided to fewer than 25% of cardiac arrest victims,<sup>6,21,32</sup> and it is known that delivering shocks can be difficult for lay rescuers.<sup>33</sup> Considering the difficulties of performing CPR and delivering shocks and the evidence that supports the effectiveness of bystander-initiated, compression-only CPR,<sup>24,34,35</sup> further efforts to strengthen the first 3 links in the chain of survival by use of compression-only CPR might be more feasible, as recommended recently by the American Heart Association.<sup>36</sup>

## Study Limitations

An important limitation of the present study was the potential for bias on the basis of its observational design. As with all multisite epidemiological studies, data integrity, validity, and ascertainment bias are also potential limitations. We believe that the use of uniform data collection and consistent definitions based on Utstein-style guidelines for reporting cardiac arrest, the time synchronization process, the large sample size, and a population-based design that included all known adults with OHCA in Osaka Prefecture minimize these potential sources of bias.

In the present study, we had no data at the hospital level, such as the prevalence of postresuscitation care, including therapeutic hypothermia. The incremental benefit of advanced hospital care should be investigated further.

## Conclusions

Data from a large-scale population-based cohort in Osaka demonstrate a continuous increase in survival after witnessed OHCA of presumed cardiac origin with improvements in the chain of survival. An incremental benefit of some ALS procedures on survival after OHCA is also suggested.

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## Disclosures

None.

## References

- ECC Committee, Subcommittees, and Task Forces of the American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2005;112(suppl):IV-1–IV-203.
- Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. *Circulation*. 2001;104:2158–2163.
- Centers for Disease Control and Prevention. Web-based Injury Statistics Query and Reporting System (WISQARS). National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. Available at: <http://www.cdc.gov/nipc/wisqars>. Accessed January 22, 2008.
- Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, Rea T, Lowe R, Brown T, Dreyer J, Davis D, Idris A, Stiell I; Resuscitation Outcomes Consortium Investigators. Regional variation in out-of-hospital cardiac arrest incidence and outcome. *JAMA*. 2008;300:1423–1431.
- Rea TD, Eisenberg MS, Becker LJ, Murray JA, Hearne T. Temporal trends in sudden cardiac arrest: a 25-year emergency medical services perspective. *Circulation*. 2003;107:2780–2785.
- Herlitz J, Bang A, Gunnarsson J, Engdahl J, Karlson BW, Lindqvist J, Waagstein L. Factors associated with survival to hospital discharge among patients hospitalised alive after out of hospital cardiac arrest: change in outcome over 20 years in the community of Goteborg, Sweden. *Heart*. 2003;89:25–30.
- Gillum RF. Sudden coronary death in the United States: 1980–1985. *Circulation*. 1989;79:756–765.
- Higgins MW, Luepker RV. *Trends in Coronary Heart Disease Mortality: The Influence of Medical Care*. New York, NY: Oxford University Press; 1988.
- Rosamond WD, Chambless LE, Folsom AR, Cooper LS, Conwill DE, Clegg L, Wang C-H, Heiss G. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. *N Engl J Med*. 1998;339:861–867.
- Cummins RO, Ornato JP, Thies WH, Pepe PE. Improving survival from sudden cardiac arrest: the “chain of survival” concept. *Circulation*. 1991;83:1832–1847.
- Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. *N Engl J Med*. 2000;343:1206–1209.
- Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, Zalenski R, Becker LB, Schron EB, Proschan M; Public Access Defibrillation Trial Investigators. Public-access defibrillation and survival after out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351:637–646.
- Herlitz J, Andersson E, Bang A, Engdahl J, Holmberg M, Lindqvist J, Karlson BW, Waagstein L. Experiences from treatment of out-of-hospital cardiac arrest during 17 years in Goteborg. *Eur Heart J*. 2000;21:1251–1258.
- Stiell IG, Wells GA, Field BJ, Spaite DW, De Maio VJ, Ward R, Munkley DP, Lyver MB, Luinstra LG, Campeau T, Maloney J, Dagnone E. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS Study Phase II. *JAMA*. 1999;281:1175–1181.
- Eckstein M, Stratton SJ, Chan LS. Cardiac Arrest Resuscitation Evaluation in Los Angeles: CARE-LA. *Ann Emerg Med*. 2005;45:504–509.
- Lombardi G, Gallagher J, Gennis P. Outcome of out-of-hospital cardiac arrest in New York City: the Pre-Hospital Arrest Survival Evaluation (PHASE) Study. *JAMA*. 1994;271:678–683.
- Becker LB, Ostrander MP, Barrett J, Kondos GT. Outcome of CPR in a large metropolitan area: where are the survivors? *Ann Emerg Med*. 1991;20:355–361.
- Pepe PE, Abramson NS, Brown CG. ACLS: does it really work? *Ann Emerg Med*. 1994;23:1037–1041.
- Nichol G, Stiell IG, Laupacis A, Pham B, De Maio VJ, Wells GA. A cumulative meta-analysis of the effectiveness of defibrillator-capable emergency medical services for victims of out-of-hospital cardiac arrest. *Ann Emerg Med*. 1999;34:517–525.
- Nichol G, Detsky AS, Stiell IG, O'Rourke K, Wells GA, Laupacis A. Effectiveness of emergency medical services for victims of out-of-hospital cardiac arrest: a metaanalysis. *Ann Emerg Med*. 1996;27:700–710.
- Stiell IG, Wells GA, Field B, Spaite DW, Nesbitt LP, De Maio VJ, Nichol G, Cousineau D, Blackburn J, Munkley D, Luinstra-Toohy L, Campeau T, Dagnone E, Lyver M. Advanced cardiac life support in out-of-hospital cardiac arrest. *N Engl J Med*. 2004;351:647–656.
- Iwami T, Hiraide A, Nakanishi N, Hayashi Y, Nishiuchi T, Yukioka H, Yoshiya I, Sugimoto H. Age and sex analyses of out-of-hospital cardiac arrest in Osaka, Japan. *Resuscitation*. 2003;57:145–152.
- Iwami T, Hiraide A, Nakanishi N, Hayashi Y, Nishiuchi T, Uejima T, Morita H, Shigemoto T, Ikeuchi H, Matsusaka M, Shinya H, Yukioka H, Sugimoto H. Outcome and characteristics of out-of-hospital cardiac arrest according to location of arrest: a report from a large-scale, population-based study in Osaka, Japan. *Resuscitation*. 2006;69:221–228.
- Iwami T, Kawamura T, Hiraide A, Berg RA, Hayashi Y, Nishiuchi T, Kajino K, Yonemoto N, Yukioka H, Sugimoto H, Kakuchi H, Sase K, Yokoyama H, Nonogi H. Effectiveness of bystander-initiated cardiac-only resuscitation for patients with out-of-hospital cardiac arrest. *Circulation*. 2007;116:2900–2907.

25. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, Halperin H, Handley A, Herlitz J, Hickey R, Idris A, Kloeck W, Larkin GL, Mancini ME, Mason P, Mears G, Monsieurs K, Montgomery W, Morley P, Nichol G, Nolan J, Okada K, Perlman J, Shuster M, Steen PA, Sterz F, Tibballs J, Timmerman S, Truitt T, Zideman D. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). *Circulation*. 2004;110:3385–3397.
26. Mitchell RG, Guly UM, Rainer TH, Robertson CE. Can the full range of paramedic skills improve survival from out of hospital cardiac arrests? *J Accid Emerg Med*. 1997;14:274–277.
27. Guly UM, Mitchell RG, Cook R, Steedman DJ, Robertson CE. Paramedics and technicians are equally successful at managing cardiac arrest outside hospital. *BMJ*. 1995;310:1091–1094.
28. Rainer TH, Marshall R, Cusack S. Paramedics, technicians, and survival from out of hospital cardiac arrest. *J Accid Emerg Med*. 1997;14:278–282.
29. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. *Circulation*. 1997;96:3308–3313.
30. Soo LH, Gray D, Young T, Skene A, Hampton JR. Influence of ambulance crew's length of experience on the outcome of out-of-hospital cardiac arrest. *Eur Heart J*. 1999;20:535–540.
31. De Maio VJ, Stiell IG, Wells GA, Spaite DW. Optimal defibrillation response intervals for maximum out-of-hospital cardiac arrest survival rates. *Ann Emerg Med*. 2003;42:242–250.
32. Wenzel V, Krismer AC, Arntz HR, Sitter H, Stadlbauer KH, Lindner KH. A comparison of vasopressin and epinephrine for out-of-hospital cardiopulmonary resuscitation. *N Engl J Med*. 2004;350:105–113.
33. Hazinski MF, Idris AH, Kerber RE, Epstein A, Atkins D, Tang W, Lurie K; American Heart Association Emergency Cardiovascular Committee; Council on Cardiopulmonary, Perioperative, and Critical Care; Council on Clinical Cardiology. Lay rescuer automated external defibrillator ("public access defibrillation") programs: lessons learned from an international multicenter trial: advisory statement from the American Heart Association Emergency Cardiovascular Committee; the Council on Cardiopulmonary, Perioperative, and Critical Care; and the Council on Clinical Cardiology. *Circulation*. 2005;111:3336–3340.
34. SOS-KANTO study group. Cardiopulmonary resuscitation by bystanders with chest compression only (SOS-KANTO): an observational study. *Lancet*. 2007;369:920–926.
35. Bohm K, Rosenqvist M, Herlitz J, Hollenberg J, Svensson L. Survival is similar after standard treatment and chest compression only in out-of-hospital bystander cardiopulmonary resuscitation. *Circulation*. 2007;116:2908–2912.
36. Sayre MR, Berg RA, Cave DM, Page RL, Potts J, White RD. Hands-only (compression-only) cardiopulmonary resuscitation: a call to action for bystander response to adults who experience out-of-hospital sudden cardiac arrest: a science advisory for the public from the American Heart Association Emergency Cardiovascular Care Committee. *Circulation*. 2008;117:2162–2167.

### CLINICAL PERSPECTIVE

This large, population-based study covering 8.8 million residents and ranging from 1998 to 2006 demonstrates a continuous increase in out-of-hospital cardiac arrest survival with improvements in the "chain of survival." Among 42 873 resuscitation-attempted adult out-of-hospital cardiac arrests, 8782 bystander-witnessed arrests of presumed cardiac origin were analyzed. During the study period, the proportion of those who received bystander-initiated cardiopulmonary resuscitation increased from 19% to 36%, and the median time interval from collapse to initiation of cardiopulmonary resuscitation decreased from 9 to 7 minutes. The median interval from collapse to first shock decreased from 19 to 9 minutes because of improvements in the emergency medical service response. Neurologically intact 1-month survival after all rhythms and after ventricular fibrillation of witnessed cardiac arrests increased from 2% to 6% and from 6% to 17%, respectively. The concept that survival improves as response times decrease and bystander efforts increase is widely accepted, but few reports have shown the potential impact of ongoing efforts to improve the chain of survival. In multivariable analyses, earlier cardiopulmonary resuscitation (odds ratio per minute 0.89) and earlier intubation (odds ratio per minute 0.96) were associated with better neurological outcome. For ventricular fibrillation, only earlier shock was associated with better outcome (odds ratio 0.84). The incremental benefit of early advanced care on out-of-hospital cardiac arrest survival is also suggested. Emphasis should be placed on increasing bystander-initiated cardiopulmonary resuscitation and integrating such changes with improvements in advanced life support to save more lives.

## Continuous Improvements in "Chain of Survival" Increased Survival After Out-of-Hospital Cardiac Arrests: A Large-Scale Population-Based Study

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