

# BMJ Open

## Epidemiology and outcome of out-of-hospital cardiac arrest with non-cardiac origin in Osaka: a population-based study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-006462
Article Type:	Research
Date Submitted by the Author:	25-Aug-2014
Complete List of Authors:	Kitamura, Tetsuhisa; Osaka University, Graduate School of Medicine Kiyohara, Kosuke; Tokyo Women's Medical University, Sakai, Tomohiko; Osaka University, Department of Traumatology and Acute Critical Medicine Iwami, Taku ; Kyoto University , Health Service Nishiyama, Chika; Kyoto University, Department of Critical Care Nursing Kajino, Kentaro; Osaka National Hospital, Traumatology and Critical Care Medical Center Nishiuchi, Tatsuya; Kinki University, Department of Acute Medicine Hayashi, Yasuyuki; Osaka Saiseikai Senri Hospital, Senri Critical Care Medical Center Katayama, Yusuke; Osaka University, Department of Traumatology and Acute Critical Medicine Yoshiya, Kazuhisa; Osaka University, Department of Traumatology and Acute Critical Medicine Shimazu, Takeshi; Osaka University, Department of Traumatology and Acute Critical Medicine
<b>Primary Subject Heading</b>:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Cardiovascular medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

SCHOLARONE™  
Manuscripts

1 **Epidemiology and outcome of out-of-hospital cardiac arrest with**  
2 **non-cardiac origin in Osaka: a population-based study**

3  
4 Tetsuhisa Kitamura,<sup>1</sup> Kosuke Kiyohara,<sup>2</sup> Tomohiko Sakai,<sup>3</sup> Taku Iwami,<sup>4</sup> Chika Nishiyama,<sup>5</sup>  
5 Kentaro Kajino,<sup>6</sup> Tatsuya Nishiuchi,<sup>7</sup> Yasuyuki Hayashi,<sup>8</sup> Yusuke Katayama,<sup>3</sup> Kazuhisa  
6 Yoshiya,<sup>3</sup> Takeshi Shimazu<sup>3</sup>

7  
8 **Author affiliations**

9 <sup>1</sup>Division of Environmental Medicine and Population Sciences, Department of Social and  
10 Environmental Medicine, Graduate School of Medicine, Osaka University, Japan

11 <sup>2</sup>Department of Public Health, Tokyo Women's Medical University, Japan

12 <sup>3</sup>Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School  
13 of Medicine, Japan

14 <sup>4</sup>Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto, Japan

15 <sup>5</sup>Department of Critical Care Nursing, Graduate School of Medicine and School of Health  
16 Sciences, Kyoto University, Japan

17 <sup>6</sup>Traumatology and Critical Care Medical Center, National Hospital Organization Osaka  
18 National Hospital, Japan

1  
2  
3  
4  
5  
6 1 <sup>7</sup>Department of Acute Medicine, Kinki University Faculty of Medicine, Japan  
7

8  
9 2 <sup>8</sup>Senri Critical Care Medical Center, Osaka Saiseikai Senri Hospital, Japan  
10

11  
12 3

13  
14 4 **Correspondence to**

15  
16  
17 5 Taku Iwami MD, PhD

18  
19  
20 6 Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501  
21

22  
23 7 Phone: +81-75-753-2426; Fax: +81-75-753-2424  
24

25  
26 8 E-mail: iwamit@e-mail.jp  
27

28  
29 9  
30

31  
32 10 **Total word count:** 3903 words (main text). **Abstract:** 277 words.  
33

34  
35 11  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 ABSTRACT**  
7

8  
9 **2 Objectives:** To evaluate epidemiological characteristics of out-of-hospital cardiac  
10  
11  
12 3 arrests (OHCAs) by detailed non-cardiac cause and factors associated with the  
13  
14 4 outcomes after OHCAs with non-cardiac origin.  
15

16  
17  
18 5 **Design:** A prospective, population-based observational study.  
19

20  
21 6 **Setting:** The Utstein Osaka Project.  
22

23  
24 7 **Participants:** 14,164 adult patients with OHCAs due to non-cardiac origin who were  
25  
26 8 resuscitated by emergency-medical-service personnel or bystanders, and then were  
27  
28 9 transported to medical institutions from January 2005 to December 2011.  
30

31  
32 10 **Primary outcome measures:** One-month survival after OHCA. Multiple logistic  
33  
34 11 regression analysis was used to assess factors that were potentially associated with the  
35  
36 12 outcome.  
37

38  
39  
40 13 **Results:** During the study period, the one-month survival rate was 5.3% (755/14,164).  
41  
42 14 The proportion of one-month survival was 6.2% (510/8239) in external causes, 6.5%  
43  
44 15 (94/1148) in respiratory diseases, 0.8% (11/1309) in malignant tumors, 4.9% (55/1114)  
45  
46 16 in cerebrovascular diseases, and 4.1% (85/2054) in others. As for external causes, the  
47  
48 17 proportion of one-month survival was 14.3% (382/2670) in asphyxia, 4.2% (84/1999)  
49  
50 18 in hanging, 0.7% (9/1300) in fall, 1.1% (12/1062) in drowning, 1.6% (12/765) in  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 traffic injury, 3.7% (7/187) in drug overuse, and 1.6% (4/256) in unclassified external  
2 causes. In a multivariate analysis, arrests witnessed by bystanders, good activities of  
3 daily living before arrests, ventricular fibrillation arrests, public places, intravenous  
4 fluid, and early emergency-medical-service response time were significant predictors  
5 for one-month outcome after OHCA with cardiac origin. The proportion of one-month  
6 survival of the whole OHCA with non-cardiac origin did not significantly increase  
7 (from 4.3% [86/2023] in 2005 to 4.9% [105/2126] in 2011) and the adjusted odds ratio  
8 for one-increment of year was 1.01 (95% confidence interval 0.97-1.06).

9 **Conclusions:** From a large OHCA registry in Osaka, we demonstrated that one-month  
10 survival after OHCA with non-cardiac origin was poor and stable.

11

1  
2  
3  
4  
5  
6 **1 Strengths and limitations of this study**  
7

8  
9 ■ This study showed that one-month survival after OHCA with non-cardiac origin  
10  
11 was poor and the survival trends did not improve year-by-year in Osaka during the  
12  
13 study period from 2005 to 2011. In addition, the survival exceedingly differed by  
14  
15 detailed non-cardiac origin.  
16  
17  
18  
19

20  
21 ■ The category of presumed non-cardiac causes is made clinically, as per the  
22  
23 Utstein-style international guidelines for cardiac arrest data reporting.  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 INTRODUCTION

2 Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the  
3 industrialized world.<sup>1-4</sup> Although improvements in the chain of survival including the  
4 development of a public-access defibrillation system and revisions to cardiopulmonary  
5 resuscitation (CPR) guidelines have led to increased survival after OHCA with cardiac  
6 origin in some communities,<sup>5-7</sup> the outcome after OHCA with non-cardiac origin  
7 remains generally poor.<sup>7-13</sup>

8 Importantly, 20% to 40% of adult OHCA were reportedly of non-cardiac origin.<sup>7-13</sup>  
9 However, epidemiological characteristics of OHCA with non-cardiac origin have not  
10 been sufficiently investigated as much as those of OHCA with cardiac origin.  
11 Therefore, the evaluation of characteristics, trends, and outcomes by detailed  
12 non-cardiac cause and understanding the factors associated with the outcomes are  
13 needed to improve the survival after OHCA with non-cardiac origin.

14 The Utstein Osaka Project is a large prospective population-based cohort study of  
15 OHCA in Osaka, Japan, covering about 8.8 million residents.<sup>5</sup> During the 7 years from  
16 2005 to 2011, we enrolled approximately 14,000 OHCA with non-cardiac origin  
17 before emergency-medical-service (EMS) arrival. The present study aimed to evaluate  
18 the epidemiological characteristics of OHCA by detailed non-cardiac cause. In

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 addition, we evaluated factors associated with the outcomes after OHCA with  
2 non-cardiac origin in a multivariate analysis.  
3

For peer review only



## 1 METHODS

### 2 Study design and setting

3 The Utstein Osaka Project is a prospective, population-based registry of OHCA that is  
4 based on the standardized Utstein style.<sup>14,15</sup> This study enrolled adult patients aged  
5 =>20 years suffering OHCAs with non-cardiac origin before EMS arrival, who were  
6 resuscitated by EMS personnel or bystanders, and were transported to medical  
7 institutions in Osaka Prefecture from January 1, 2005 to December 31, 2011.

8 Cardiac arrest was defined as the cessation of cardiac mechanical activity as  
9 confirmed by the absence of signs of circulation.<sup>14,15</sup> In this study, the arrests were  
10 classified into those of presumed cardiac origin and non-cardiac origin, the latter  
11 resulting from external causes, respiratory diseases, malignant tumors, cerebrovascular  
12 diseases, and any other non-cardiac causes. Furthermore, external causes were divided  
13 into the seven categories: asphyxia, hanging, fall, drowning, traffic injury, drug overuse,  
14 and unclassified external causes. These diagnoses were made clinically by the  
15 physician in charge, working in collaboration with the EMS personnel.

16

### 17 EMS organization in Osaka

18 Details of the EMS system in Osaka were described previously.<sup>5</sup> Osaka is the second

1  
2  
3  
4  
5  
6 1 largest prefecture in Japan with a population of approximately 8.8 million inhabitants  
7  
8  
9 2 in an area of 1892 km<sup>2</sup>. In Osaka, there are 34 fire stations with emergency dispatch  
10  
11 3 centers. The EMS system is operated by the local fire stations. When called, an  
12  
13 4 ambulance is dispatched from the nearest fire station. Emergency services are provided  
14  
15 5 24 hours each day by them, which is single-tiered in 32 stations and two-tiered in two  
16  
17 6 stations. The latter uses medics followed by physicians.  
18  
19  
20  
21  
22

23 7 Most highly-trained prehospital emergency care providers are called Emergency  
24  
25 8 Life-Saving Technicians (ELSTs). Usually, each ambulance has a crew of three  
26  
27 9 emergency providers including at least one ELST. They were allowed to insert an  
28  
29 10 intravenous line and an adjunct airway, and to use a semi-automated external  
30  
31 11 defibrillator for OHCA patients. Specially trained ELSTs were permitted to tracheal  
32  
33 12 intubation since July 2004 and administer intravenous epinephrine since April 2006.  
34  
35  
36  
37  
38  
39

40 13 Do-not-resuscitate (DNR) orders or living wills are not generally accepted in Japan.  
41  
42 14 EMS providers are not permitted to terminate resuscitation in the field. Therefore,  
43  
44 15 almost patients with OHCA who were treated by EMS personnel were transported to a  
45  
46 16 hospital and enrolled in the Utstein Osaka Project, excluding those with decapitation,  
47  
48 17 incineration, decomposition, rigor mortis, or dependent cyanosis.  
49  
50  
51  
52  
53  
54

55 18  
56  
57  
58  
59  
60

## 1 **CPR and AED training for the general public**

2 The use of an automated external defibrillator (AED) by citizens was permitted legally  
3 in July 2004. In Osaka, approximately 14,000 citizens per year participated in the CPR  
4 training programs, consisting of conventional CPR including chest compressions,  
5 mouth-to-mouth ventilation, and AED usage by local fire departments, the Japan Red  
6 Cross, Inc., and the Osaka Life Support Association.<sup>5</sup> All EMS providers perform CPR  
7 according to the Japanese CPR guidelines.<sup>4</sup>

## 9 **Data collection and quality control**

10 Data collection were prospectively conducted using a form that included data  
11 recommended in the Utstein-style reporting guidelines for cardiac arrests.<sup>14,15</sup> These  
12 data included gender, age, first documented cardiac rhythm, witness status, location of  
13 arrests, activity of daily living (ADL) before arrests, time-courses of resuscitation, type  
14 of bystander-initiated CPR, public-access AED use, intravascular fluid, tracheal  
15 intubation, and intravascular epinephrine as well as prehospital return of spontaneous  
16 circulation (ROSC), total ROSC, one-month survival, and neurological status one  
17 month after the event. First documented rhythm was recorded and diagnosed by the  
18 EMS personnel with semi-automated defibrillators on the scene, and confirmed by the

1 physician who was responsible for the on-line medical direction. Bystander CPR  
2 included chest compression-only CPR and conventional CPR with rescue breathing. A  
3 series of EMS times of call receipt, vehicle arrival at the scene, contact with patients,  
4 initiation of CPR, defibrillation by EMS, and hospital arrival were recorded  
5 automatically at the dispatch center.

6 The data form was completed by the EMS personnel in cooperation with the  
7 physicians in charge of the patients, and the data were integrated into the registry  
8 system on the Information Center for Emergency Medical Services of Osaka, and then  
9 checked by the investigators. If the data sheet was incomplete, the relevant EMS  
10 personnel were contacted and questioned for data completion.

11 All survivors suffering OHCA were followed up for up to one-month after the event  
12 by the EMS personnel in charge. One-month neurological outcomes were determined  
13 by the physician responsible for treating the patient, using the cerebral performance  
14 category (CPC) scale: category 1, good cerebral performance; category 2, moderate  
15 cerebral disability; category 3, severe cerebral disability; category 4, coma or  
16 vegetative state; and category 5, death.<sup>14,15</sup>

## 18 **Outcome measures**

1 The main outcome measure was one-month survival. Secondary outcome measures  
2 included prehospital and total ROSCs, admission to hospital, and one-month survival  
3 with neurologically favorable outcome. Neurologically intact outcome was defined as  
4 CPC category 1 or 2.<sup>14,15</sup>

## 6 **Statistical analysis**

7 In this study, patient and EMS characteristics of OHCA with non-cardiac origin and  
8 their outcomes were compared between the groups using unpaired analysis of variance  
9 for numerical variables, and chi-square test or Fisher's exact test for categorical  
10 variables by cause of arrest. First, non-cardiac causes were divided into the following  
11 five groups; external causes, respiratory diseases, malignant tumors, cerebrovascular  
12 diseases, and any other non-cardiac causes. Next, external causes were further divided  
13 into asphyxia, hanging, fall, drowning, traffic injury, drug overuse, and unclassified  
14 external causes. Age-adjusted annual incidence of OHCA by non-cardiac origin was  
15 calculated by the direct method using 2005 census data and 1985 Japanese model  
16 population.<sup>16,17</sup> Poisson regression models for the trends in the incidence were used.  
17 Multiple logistic regression analysis assessed the factors associated with one-month  
18 survival and neurological favorable outcome, and adjusted odds ratios (AORs) and

1  
2  
3  
4  
5  
6 1 their 95% confidence intervals (CIs) were calculated. As potential confounders, factors  
7  
8  
9 2 that were biologically essential and considered to be associated with clinical outcomes  
10  
11  
12 3 were taken in the multivariable analyses.<sup>7</sup> These variables included age (20-64, ≥65  
13  
14 4 years old), gender (men, women), witness status (none, witnessed by bystanders), ADL  
15  
16  
17 5 before arrests (good, other), first documented rhythm (VF, non-VF), bystander CPR  
18  
19  
20 6 status (none, compression-only CPR, conventional CPR), type of non-cardiac causes  
21  
22  
23 7 (the 11 categories described above), location of arrests (homes, public places, work  
24  
25  
26 8 places, health care facilities, others), intravascular fluid (yes, no), intubation (yes, no),  
27  
28  
29 9 epinephrine (yes, no), EMS response time (call to contact with patients), and year of  
30  
31  
32 10 arrest.

33  
34  
35 11 All statistical analyses were performed using the SPSS statistical package ver21.0J  
36  
37  
38 12 (IBM Corp. Armonk, NY). All of the tests were 2-tailed and *P* values of <0.05 were  
39  
40  
41 13 considered statistically significant.

42  
43  
44 14

## 1 RESULTS

2 Figure 1 shows an overview of the study patients based on the Utstein template. A total  
3 of 47,735 adult arrests were documented during these seven years. Resuscitation was  
4 attempted in 43,845, and 15,505 of them were of non-cardiac origin. Excluding 1341  
5 victims who were witnessed by EMS (arrests after EMS arrival), 14,164 (5561 in  
6 bystander-witnessed cases and 8603 in non-witnessed cases) were eligible for our  
7 analyses. Among these arrests, 8239 (58.2%) were due to external causes, 1448  
8 (10.2%) respiratory diseases, 1309 (9.2%) malignant tumors, 1114 cerebrovascular  
9 (7.9%) diseases, and 2054 (14.5%) others. Among external causes, 2670 (16.5%) were  
10 of asphyxia, 1999 (14.1%) hanging, 1300 (9.2%) fall, 1062 (7.5%) drowning, 765  
11 (5.4%) traffic injury, and 256 (1.8%) unclassified external cause.

12 The age-adjusted annual incidence rates per 100,000 persons by non-cardiac cause  
13 were calculated over time (Table 1). The incidence rate of OHCA with external  
14 causes significantly increased from 12.4 in 2005 to 13.3 in 2011 (P for trend=0.024).  
15 The incidence rate significantly decreased among OHCA patients with respiratory  
16 diseases (from 2.2 in 2005 to 1.6 in 2011, P for trend=0.018) and cerebrovascular  
17 diseases (from 2.0 in 2005 to 1.3 in 2011, P for trend<0.001).

18 Patient and EMS characteristics of OHCA with non-cardiac origin according to the

1  
2  
3  
4  
5  
6 1 cause are shown in Table 2, and their outcomes in Table 4. The mean age of all OHCA  
7  
8  
9 2 patients with non-cardiac origin was 66.8 years and males were 58.0%. The proportion  
10  
11  
12 3 of bystander-witnessed arrests, ADL before arrests, first documented rhythm, type of  
13  
14 4 bystander CPR, and advanced life supports such as intravascular fluid, intubation, and  
15  
16  
17 5 epinephrine exceedingly varied between the five groups. In the whole patients, the rate  
18  
19  
20 6 of one-month survival and neurologically favorable outcome was 5.3% and 1.3%. The  
21  
22  
23 7 proportion of one-month survival was 6.2% in external causes, 6.5% in respiratory  
24  
25  
26 8 diseases, 0.8% in malignant tumors, 4.9% in cerebrovascular diseases, and 4.1% in  
27  
28  
29 9 others. Furthermore, patient and EMS characteristics of OHCAs in external causes are  
30  
31  
32 10 shown in Table 3, and their outcomes in Table 5. The characteristics and outcomes  
33  
34  
35 11 varied between the seven groups. The proportion of one-month survival was 14.3% in  
36  
37  
38 12 asphyxia, 4.2% in hanging, 0.7% in fall, 1.1% in submersion, 1.6% in traffic injury,  
39  
40  
41 13 3.7% in drug overuse, and 1.6% in unclassified external cause.

42  
43  
44 14 Table 6 shows factors contributing to one-month survival and neurologically  
45  
46  
47 15 favorable outcome after OHCAs with non-cardiac origin. In one-month survival,  
48  
49  
50 16 arrests witnessed by bystanders (AOR 4.13, 95% CI 3.35-5.09), good ADL before  
51  
52  
53 17 arrests (AOR 1.23, 95% CI 1.03-1.47), VF as first documented rhythm (AOR 2.04,  
54  
55  
56 18 95% CI 1.42-2.92), public places (AOR 1.45, 95% CI 1.10-1.91), intravenous fluid  
57  
58  
59  
60



1 (AOR 1.45, 95% CI 1.14-1.84), and early EMS response time (AOR for one-increment  
2 of minute 1.45, 95% CI 1.10-1.91) were associated with improving outcome. However,  
3 type of bystander CPR, intubation, and epinephrine were not associated with better  
4 outcome. Compared with asphyxia, the AORs were significantly lower in respiratory  
5 diseases (0.51, 95% CI 0.40-0.65), malignant tumors (0.06, 95% CI 0.03-0.11),  
6 cerebrovascular disease (0.27, 95% CI 0.20-0.38), hanging (0.56, 95% CI 0.41-0.77),  
7 fall (0.03, 95% CI 0.01-0.06), drowning (0.16, 95% CI 0.09-0.29), and traffic injury  
8 (0.05, 95% CI 0.03-0.10). The proportion of one-month survival of the whole OHCA  
9 with non-cardiac origin did not significantly increase (from 4.3% [86/2023] in 2005 to  
10 4.9% [105/2126] in 2011) and the AOR for one-increment of year was 1.01 (95% CI  
11 0.97-1.06). The AORs of neurologically favorable outcome after OHCA with  
12 non-cardiac origin were almost similar to those of one-month survival.

13

1  
2  
3  
4  
5  
6 **1 DISCUSSION**  
7

8  
9 2 The extensive OHCA registry in Osaka showed that one-month survival after OHCA  
10  
11 3 with non-cardiac origin was poor and the survival trends did not improve year-by-year.

12  
13  
14 4 In addition, the survivals differed by detailed non-cardiac origin. To further improve  
15  
16 5 survival after OHCA, sufficient attention should be paid to the epidemiological  
17  
18 6 characteristics of OHCA with non-cardiac origin as much as those of OHCA with  
19  
20 7 cardiac origin, and this study describing the actual situation regarding the incidence  
21  
22 8 and outcome of OHCA with non-cardiac origin provides valuable information to  
23  
24 9 improve the survival.  
25  
26  
27  
28  
29  
30  
31

32 10 Our study observed that the outcomes of OHCA with non-cardiac origin were poor  
33  
34 11 and stable during the seven years. In a previous study in Japan, neurologically  
35  
36 12 favorable outcome of bystander-witnessed OHCA with non-cardiac origin increased  
37  
38 13 from 2005 to 2011, but the absolute survival was very low,<sup>7</sup> and this result was similar  
39  
40 14 with ours. Improving the outcome of OHCA with non-cardiac origin poses an  
41  
42 15 important problem in resuscitation science because 20~40% of adult OHCA are of  
43  
44 16 non-cardiac origin.<sup>7-13</sup> In addition, the survivals exceedingly differed by detailed  
45  
46 17 non-cardiac origin, which also suggests the need and importance of an origin-specific  
47  
48 18 strategy for improving the outcomes.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 We also showed that the OHCA incidence trends differed by detailed non-cardiac  
2 origin. For instance, the incidence rate of OHCA due to cerebrovascular diseases  
3 significantly decreased during the study period. Although the reasons for the decrement  
4 were unclear, better blood pressure control and decreasing smoking rate in recent years  
5 of Japan might be one of the possible explanations for this phenomenon.<sup>18</sup> In fact, the  
6 numbers of stroke patients in Japan has also been decreasing.<sup>19</sup> On the other hand, the  
7 incidence rates of OHCA with external causes increased and the outcomes after  
8 OHCA with external causes excluding asphyxia were miserable. Therefore, most  
9 importantly, more efforts should focus on prevention of OHCA with external causes  
10 because many of them are preventable.<sup>1-4</sup>

11 In a multivariable analysis, intravenous fluid administration was associated with  
12 better one-month survival after OHCA with non-cardiac origin. In preceding studies,  
13 prehospital intravenous fluid for OHCA including both cardiac and non-cardiac  
14 origins was not associated with the improved outcome,<sup>20</sup> whereas intravenous access  
15 were associated with a reduction in hospital mortality among non-injured, non-cardiac  
16 arrest patients.<sup>21</sup> Thus, the effects of fluid administration on prehospital emergency  
17 patients were under debate, and further investigations by other cohorts or randomized  
18 controlled trials are needed to confirm these associations.

1  
2  
3  
4  
5  
6 1 In this study, a multivariate analysis also underscored that either bystander-initiated  
7  
8  
9 2 chest compression-only CPR or conventional CPR with rescue breathing was not  
10  
11  
12 3 effective for OHCA with non-cardiac origin. From a nationwide study focused on  
13  
14  
15 4 43,000 bystander-witnessed OHCA with non-cardiac origin, we demonstrated that  
16  
17  
18 5 conventional CPR with rescue breathing had an incremental benefit for OHCA with  
19  
20  
21 6 non-cardiac origin, but the impact on the overall survival after OHCA was small.<sup>8</sup>  
22  
23  
24 7 Considering these results, the effectiveness of bystander CPR on OHCA with cardiac  
25  
26  
27 8 non-cardiac origin might be limited. However, as recommended in the CPR  
28  
29  
30 9 guidelines,<sup>1-4</sup> bystander CPR plays a key role in the “chain of survival” and increasing  
31  
32  
33 10 the proportion of bystander CPR for OHCA patients is important.

34  
35 11 Furthermore, factors such as arrests witnessed by bystanders and earlier EMS  
36  
37  
38 12 response time were also independent predictors of better outcome after OHCA with  
39  
40  
41 13 non-cardiac origin in a multivariate analysis. This would indicate the importance of an  
42  
43  
44 14 early EMS activation in the chain of survival<sup>1-4</sup> and suggests that activating the EMS  
45  
46  
47 15 system quickly leads to improving the outcomes after OHCA with non-cardiac origin.  
48  
49  
50 16 In addition, the verification of the effects on prehospital emergency care as well as  
51  
52  
53 17 in-hospital treatment is essential to improve survival after OHCA with non-cardiac  
54  
55  
56 18 origin.

1 The present study has some inherent limitations. First, the category of presumed  
2 cardiac or non-cardiac causes is made clinically, as per the Utstein-style international  
3 guidelines for cardiac arrest data reporting.<sup>14,15</sup> Second, information on post-arrest care  
4 is lacking. In-hospital treatment (e.g., hemodynamic support, cardiovascular  
5 intervention, induced hypothermia) might affect survival after OHCA.<sup>22</sup> Third,  
6 unmeasured confounding factors may have influenced the association between OHCAs  
7 with non-cardiac origin and the outcome.

## 9 **CONCLUSION**

10 The large OHCA registry in Osaka demonstrated that one-month survival after OHCAs  
11 with non-cardiac origin was poor, the survival trends did not improve year-by-year, and  
12 the survivals differed by detailed non-cardiac origin. Further monitoring and discussion  
13 for epidemiology and outcome of OHCAs with non-cardiac origin are warranted to  
14 improve survival after OHCA in this group.

15

1  
2  
3  
4  
5  
6 **1 Acknowledgments**  
7

8  
9 2 We are deeply indebted to all of the EMS personnel and concerned physicians in Osaka  
10  
11 3 Prefecture, and the Osaka Medical Association for their indispensable cooperation and  
12  
13 4 generous support. We also thank all members of the Utstein Osaka Project for their  
14  
15 5 contribution in the organization, coordination, and oversight as the steering committee.  
16  
17  
18  
19

20  
21 6

22  
23 **7 Contributors**  
24

25  
26 8 All authors (TK, KK, TS, TI, CN, KK, TN, YH, YK, KY, and TS) participated in the study  
27  
28 9 conception and design, acquisition of data, analysis and interpretation of data, drafting the  
29  
30 10 article and revising it critically for important intellectual content, and final approval of the  
31  
32 11 manuscript.  
33  
34  
35  
36  
37  
38  
39  
40

41 **13 Funding**  
42

43  
44 14 This study was supported by a scientific research grant from the Ministry of Health, Labour,  
45  
46 15 and Welfare of Japan (25112601).  
47  
48

49  
50 16

51  
52 **17 Competing interests**  
53

54  
55 18 None.  
56  
57  
58  
59  
60

1

2  
3  
4  
5  
6  
7  
8  
9 **2 Ethics approval**

10  
11  
12 3 The study was approved by the institutional review board of Osaka University with the assent  
13  
14 4 of the EMS authorities of the local governments in Osaka Prefecture.  
15  
16  
17  
18  
19

20  
21 **6 Provenance and peer review**

22  
23 7 Not commissioned; externally peer reviewed.  
24  
25  
26  
27  
28

29  
30 **9 Data sharing statement**

31  
32 10 TK had full access to all of the data in the study and takes responsibility for the integrity of the  
33  
34  
35 11 data and the accuracy of the data analysis.  
36  
37  
38  
39  
40

41 **13 Open Access**

42  
43  
44 14 This is an Open Access article distributed in accordance with the Creative Commons  
45  
46  
47 15 Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute,  
48  
49  
50 16 remix, adapt, build upon this work noncommercially, and license their derivative works on  
51  
52  
53 17 different terms, provided the original work is properly cited and the use is non-commercial.  
54  
55  
56 18 See: <http://creativecommons.org/licenses/by-nc/3.0/>  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 REFERENCES**  
7

- 8  
9 2 1. 2010 International consensus on cardiopulmonary resuscitation and emergency  
10  
11 3 cardiovascular care science with treatment recommendations. *Circulation*  
12  
13 4 2010;122:S250-605.  
14  
15  
16  
17 5 2. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and  
18  
19 6 emergency cardiovascular care. *Circulation* 2010;122:S639-946.  
20  
21  
22  
23 7 3. European Resuscitation Council Guidelines for Resuscitation 2010. *Resuscitation*  
24  
25 8 2010;81:1219-451.  
26  
27  
28  
29 9 4. 2010 Japanese guidelines for emergency care and cardiopulmonary resuscitation. 1st ed.  
30  
31 10 Tokyo: Health Shuppansha; 2011 (in Japanese).  
32  
33  
34  
35 11 5. Iwami T, Nichol G, Hiraide A, *et al.* Continuous improvements of chain of survival  
36  
37 12 increased survival after out-of-hospital cardiac arrests: a large-scale population-based  
38  
39 13 study. *Circulation* 2009;119:728-34.  
40  
41  
42  
43 14 6. Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation  
44  
45 15 during out-of-hospital ventricular fibrillation arrest: survival implications of guideline  
46  
47 16 changes. *Circulation* 2006;114:2760-5.  
48  
49  
50  
51  
52 17 7. Kitamura T, Iwami T, Kawamura T, *et al.* Nationwide improvements in survival from  
53  
54 18 out-of-hospital cardiac arrests in Japan. *Circulation* 2012;126:2834-43.  
55  
56  
57  
58  
59  
60



- 1  
2  
3  
4  
5  
6 1 8. Kitamura T, Iwami T, Kawamura T, *et al.* Bystander-initiated rescue breathing for  
7  
8  
9 2 out-of-hospital cardiac arrests of non-cardiac origin. *Circulation* 2010;122:293-9.  
10  
11  
12 3 9. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin.  
13  
14  
15 4 Epidemiology and outcome. *Eur Heart J* 1997;18:1122-8.  
16  
17  
18 5 10. Engdahl J, Bång A, Karlson BW, *et al.* Characteristics and outcome among patients  
19  
20  
21 6 suffering from out of hospital cardiac arrest of non-cardiac aetiology. *Resuscitation*  
22  
23  
24 7 2003;57:33-41.  
25  
26  
27 8 11. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital  
28  
29  
30 9 cardiac arrest of non-cardiac origin. *Resuscitation* 2007;72:200-7.  
31  
32  
33 10 12. Iwami T, Hiraide A, Nakanishi N, *et al.* Age and sex analyses of out-of-hospital cardiac  
34  
35  
36 11 arrest in Osaka, Japan. *Resuscitation* 2003;57:145-52.  
37  
38  
39 12 13. Engdahl J, Holmberg M, Karlson BW, *et al.* The epidemiology of out-of-hospital 'sudden'  
40  
41  
42 13 cardiac arrest. *Resuscitation* 2002;52:235-45.  
43  
44  
45 14 14. Cummins RO, Chamberlain DA, Abramson NS, *et al.* Recommended guideline for  
46  
47  
48 15 uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style: a statement  
49  
50  
51 16 for health professionals from a task force of the American Heart Association, the  
52  
53  
54 17 European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the  
55  
56  
57 18 Australian Resuscitation Council. *Circulation* 1991;84:960-75.  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 15. Jacobs I, Nadkarni V, Bahr J, *et al.* Cardiac arrest and cardiopulmonary resuscitation  
7  
8  
9 2 outcome reports: update and simplification of the Utstein templates for resuscitation  
10  
11 3 registries: a statement for healthcare professionals from a task force of the International  
12  
13 4 Liaison Committee on Resuscitation (American Heart Association, European  
14  
15 Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation  
16  
17 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
18  
19 Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.  
20  
21  
22  
23  
24  
25  
26 8 16. 2010 Population Census of Japan.  
27  
28  
29 9 [http://www.stat.go.jp/data/kokusei/2010/index.htm?utm\\_source=twitterfeed&utm\\_mediu](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter)  
30  
31  
32 10 [m=twitter](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter) (Accessed August 05, 2014) (in Japanese).  
33  
34  
35 11 17. Vital Statistics of Japan 2005. Tokyo: Health and Welfare Statistics Association; 2007.  
36  
37  
38 12 18. Hata J, Ninomiya T, Hirakawa Y, *et al.* Secular trends in cardiovascular disease and its  
39  
40  
41 13 risk factors in Japanese: half-century data from the Hisayama Study (1961-2009).  
42  
43 14 *Circulation* 2013;128:1198-205.  
44  
45  
46 15 19. 2011 Overview of Patient Survey. <http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/>  
47  
48  
49 16 (Accessed August 05, 2014) (in Japanese).  
50  
51  
52 17 20. Hagihara A, Hasegawa M, Abe T, *et al.* Prehospital lactated ringer's solution treatment  
53  
54  
55 18 and survival in out-of-hospital cardiac arrest: a prospective cohort analysis. *PLoS Med*  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 2013;10:e1001394.  
7  
8  
9 2 21. Seymour CW, Cooke CR, Hebert PL, *et al.* Intravenous access during out-of-hospital  
10  
11 3 emergency care of noninjured patients: a population-based outcome study. *Ann Emerg*  
12  
13 4 *Med* 2012;59:296-303.  
14  
15  
16  
17 5 22. Neumar RW, Nolan JP, Adrie C, *et al.* Post-cardiac arrest syndrome: epidemiology,  
18  
19 6 pathophysiology, treatment, and prognostication. A Scientific Statement from the  
20  
21 7 International Liaison Committee on Resuscitation; the American Heart Association  
22  
23 8 Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and  
24  
25 9 Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the  
26  
27 10 Council on Clinical Cardiology; the Council on Stroke. *Circulation* 2008;118:2452-8.  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

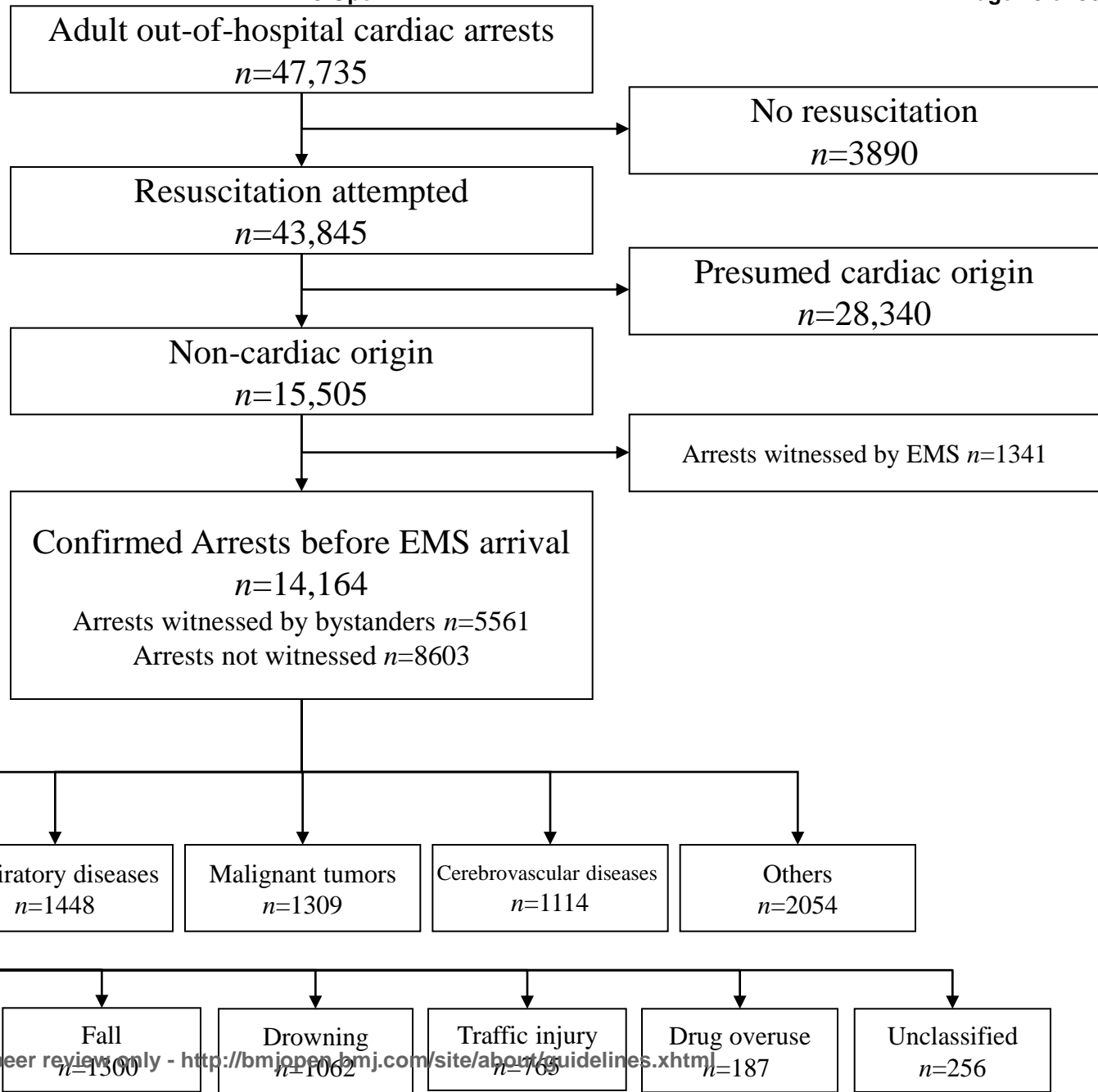
1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 **Figure Legends**

- 2 **Figure 1** Overview of EMS-treated cardiac arrests with an abridged Utstein template from  
3 January 1, 2005 to December 31, 2011. EMS, emergency medical service.

For peer review only

1 **Figure 1**  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43



**Table 1** Age-adjusted incidences of out-of-hospital cardiac arrests with non-cardiac origin according to the cause over time

	Incidence per 100,000 persons							P for trend
	2005	2006	2007	2008	2009	2010	2011	
External causes	12.4	12.3	13.2	12.8	13.2	13.3	13.3	0.024
Asphyxia	2.7	3.0	2.8	3.4	3.1	2.9	2.9	0.726
Hanging	3.4	3.4	4.1	3.4	3.7	3.9	3.9	0.158
Fall	2.4	2.5	3.1	2.4	2.9	3.0	2.7	0.396
Drowning	1.2	1.1	1.2	1.4	1.2	1.3	1.6	0.065
Traffic injury	1.6	1.5	1.4	1.4	1.4	1.5	1.4	0.229
Drug overdose	0.5	0.4	0.2	0.4	0.4	0.4	0.3	0.304
Unclassified	0.5	0.5	0.4	0.3	0.5	0.4	0.5	0.447
Respiratory diseases	2.2	1.8	1.8	1.7	1.3	1.3	1.6	0.018
Malignant tumors	1.6	1.8	1.8	1.7	1.5	1.3	1.6	0.109
Cerebrovascular diseases	2.0	1.8	1.8	1.6	1.4	1.2	1.3	< 0.001
Others	2.7	3.3	3.1	2.9	2.7	2.5	2.4	0.087

**Table 2** Patient and EMS characteristics of out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 14,164)	External causes (n = 8239)	Respiratory diseases (n = 1448)	Malignant tumors (n = 1309)	Cerebrovascular diseases (n = 1114)	Others (n = 2054)	P value*
Age, yr, mean (SD)	66.8 (19.0)	63.5 (20.5)	76.1 (14.2)	71.9 (12.0)	67.7 (14.7)	69.8 (17.6)	< 0.001
Age group, n (%)							< 0.001
Adults aged 20-64 years	5513 (38.9)	3826 (46.4)	229 (15.8)	345 (26.4)	447 (40.1)	666 (32.4)	
Elderly aged ≥65 years	8651 (61.1)	4413 (53.6)	1219 (84.2)	964 (73.6)	667 (59.9)	1388 (67.6)	
Men, n (%)	8215 (58.0)	4789 (58.1)	844 (58.3)	881 (67.3)	559 (50.2)	1142 (55.6)	< 0.001
Arrests witnessed by bystanders, n (%)	5561 (39.3)	2952 (35.8)	682 (47.1)	639 (48.8)	493 (44.3)	795 (38.7)	< 0.001
Good activities of daily living, n (%)	8522 (60.2)	5213 (63.3)	653 (45.1)	443 (33.8)	896 (80.4)	1317 (64.1)	< 0.001
First documented rhythm, n (%)							< 0.001
VF	324 (2.3)	119 (1.4)	35 (2.4)	26 (2.0)	69 (6.2)	75 (3.7)	
PEA	3356 (23.7)	1853 (22.5)	394 (27.2)	262 (20.0)	329 (29.5)	518 (25.2)	
Asystole	10196 (72.0)	6124 (74.3)	983 (67.9)	1008 (77.0)	647 (58.1)	1434 (69.8)	
Others	288 (2.0)	143 (1.7)	36 (2.5)	13 (1.0)	69 (6.2)	27 (1.3)	
Location of arrest, n (%)							< 0.001
Homes	9010 (63.6)	4435 (53.8)	1098 (75.8)	1217 (93.0)	801 (71.9)	1459 (71.0)	
Public places	2035 (14.4)	1608 (19.5)	59 (4.1)	24 (1.8)	156 (14.0)	188 (9.2)	
Work places	346 (2.4)	223 (2.7)	7 (0.5)	4 (0.3)	48 (4.3)	64 (3.1)	
Health care facilities	1505 (10.6)	904 (11.0)	248 (17.1)	55 (4.2)	63 (5.7)	235 (11.4)	
Others	1268 (9.0)	1069 (13.0)	36 (2.5)	9 (0.7)	46 (4.1)	108 (5.3)	
Public-access AED use, n (%)	13 (0.1)	4 (0.05)	2 (0.1)	0 (0.0)	5 (0.4)	2 (0.1)	0.001
Type of Bystander CPR, n (%)							< 0.001
No CPR	9023 (63.7)	5383 (65.3)	836 (57.7)	889 (67.9)	633 (56.8)	1282 (62.4)	
Chest compression-only CPR	3288 (23.2)	1811 (22.0)	408 (28.2)	297 (22.7)	283 (25.4)	489 (23.8)	
Conventional CPR with rescue breathing	1853 (13.1)	1045 (12.7)	204 (14.1)	123 (9.4)	198 (17.8)	283 (13.8)	
Intravascular fluid, n (%)	2320 (16.4)	1458 (17.7)	202 (14.0)	113 (8.6)	230 (20.6)	317 (15.4)	< 0.001
Intubation, n (%)	2639 (18.6)	1364 (16.6)	338 (23.3)	242 (18.5)	257 (23.1)	438 (21.3)	< 0.001
Epinephrine, n (%)	987 (7.0)	572 (6.9)	88 (6.1)	49 (3.7)	125 (11.2)	153 (7.4)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.9 (4.1)	8.0 (4.6)	7.7 (3.0)	7.7 (2.7)	7.7 (2.8)	7.9 (3.8)	0.003
Call to CPR by EMS, min, mean (SD)	8.5 (4.5)	8.8 (5.1)	8.1 (3.1)	8.1 (2.8)	8.2 (2.9)	8.4 (4.2)	< 0.001
Call to hospital arrival, min, mean (SD)	28.2 (8.6)	28.4 (8.6)	27.3 (8.2)	28.0 (8.9)	28.2 (8.4)	28.1 (8.7)	0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 3** Patient and EMS characteristics of out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	P value <sup>a</sup>
Age, yr, mean (SD)	77.9 (14.4)	55.6 (17.4)	47.4 (17.4)	73.1 (14.8)	52.6 (19.0)	49.9 (19.5)	58.1 (19.3)	< 0.001
Age group, n (%)								< 0.001
Adults aged 20-64 years	403 (15.1)	1136 (66.8)	1055 (81.2)	210 (19.8)	523 (68.4)	141 (75.4)	158 (61.7)	
Elderly aged ≥65 years	2267 (84.9)	663 (33.2)	245 (18.8)	852 (80.2)	242 (31.6)	46 (24.6)	98 (38.3)	
Men, n (%)	1345 (50.4)	1290 (64.5)	781 (60.1)	530 (49.9)	558 (72.9)	117 (62.6)	168 (65.6)	< 0.001
Arrests witnessed by bystanders, n (%)	1801 (67.5)	27 (1.4)	510 (39.2)	56 (5.3)	476 (62.2)	10 (5.3)	72 (28.1)	< 0.001
Good activities of daily living, n (%)	1099 (41.2)	1769 (88.5)	685 (52.7)	854 (80.4)	517 (67.6)	133 (71.1)	156 (60.9)	< 0.001
First documented rhythm, n (%)								< 0.001
VF	56 (2.1)	13 (0.7)	19 (1.5)	12 (1.1)	14 (1.8)	1 (0.5)	4 (1.6)	
PEA	960 (36.0)	198 (9.9)	274 (21.1)	72 (6.8)	259 (33.9)	20 (10.7)	70 (27.3)	
Asystole	1589 (59.5)	1775 (88.8)	985 (75.8)	970 (91.3)	469 (61.3)	160 (85.6)	176 (68.8)	
Others	65 (2.4)	13 (0.7)	22 (1.7)	8 (0.8)	23 (3.0)	6 (3.2)	6 (2.3)	
Location of arrest, n (%)								< 0.001
Homes	1596 (59.8)	1667 (83.4)	139 (10.7)	770 (72.5)	2 (0.3)	150 (80.2)	111 (43.4)	
Public places	139 (5.2)	86 (4.3)	553 (42.5)	83 (7.8)	677 (88.5)	14 (7.5)	56 (21.9)	
Workplaces	35 (1.3)	94 (4.7)	44 (3.4)	3 (0.3)	7 (0.9)	7 (3.7)	33 (12.9)	
Health care facilities	835 (31.3)	27 (1.4)	12 (0.9)	14 (1.3)	1 (0.1)	0 (0.0)	15 (5.9)	
Others	65 (2.4)	125 (6.3)	552 (42.5)	192 (18.1)	78 (10.2)	16 (8.6)	41 (16.0)	
Public-access AED use, n (%)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.214
Type of Bystander CPR, n (%)								< 0.001
No CPR	1386 (51.9)	1174 (58.7)	1191 (91.6)	608 (57.3)	673 (88.0)	154 (82.4)	197 (77.0)	
Chest compression-only CPR	748 (28.0)	549 (27.5)	93 (7.2)	281 (26.5)	74 (9.7)	23 (12.3)	43 (16.8)	
Conventional CPR with rescue breathing	536 (20.1)	276 (13.8)	16 (1.2)	173 (16.3)	18 (2.4)	10 (5.3)	16 (6.2)	
Intravascular fluid, n (%)	540 (20.2)	393 (19.7)	107 (8.2)	281 (26.5)	76 (9.9)	27 (14.4)	34 (13.3)	< 0.001
Intubation, n (%)	800 (30.0)	167 (8.4)	41 (3.2)	251 (23.6)	31 (4.1)	33 (17.6)	41 (16.0)	< 0.001
Epinephrine, n (%)	326 (12.2)	83 (4.2)	41 (3.2)	68 (6.4)	37 (4.8)	6 (3.2)	11 (4.3)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.6 (2.9)	7.8 (3.3)	7.4 (3.3)	9.4 (7.6)	7.6 (4.2)	14.2 (10.7)	9.4 (7.3)	< 0.001
Call to CPR by EMS personnel, min, mean (SD)	7.9 (3.1)	8.6 (3.9)	8.2 (3.8)	10.0 (7.5)	9.3 (5.9)	14.4 (10.0)	11.0 (8.7)	< 0.001
Call to hospital arrival, min, mean (SD)	28.6 (8.6)	28.2 (7.9)	27.5 (8.3)	29.1 (9.3)	27.1 (8.8)	32.1 (11.1)	29.5 (9.4)	< 0.001

<sup>a</sup>P values are calculated to test the homogeneity among the 7 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.



**Table 4** Outcomes after out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 1,4164)	External causes (n = 8239)	Respiratory diseases (n = 1148)	Malignat tumors (n = 1309)	Cerebrovascular diseases (n = 1114)	Others (n = 2054)	<i>P</i> value*
Prehospital ROSC, n (%)	1229 (8.7)	703 (8.5)	114 (7.9)	57 (4.4)	216 (19.4)	139 (6.8)	< 0.001
Total ROSC, n (%)	4744 (33.5)	2638 (32.0)	620 (42.8)	234 (17.9)	650 (58.3)	602 (29.3)	< 0.001
Hospital admission, n (%)	4142 (29.2)	2356 (28.6)	530 (36.6)	173 (13.2)	585 (52.5)	498 (24.2)	< 0.001
One-month survival, n (%)	755 (5.3)	510 (6.2)	94 (6.5)	11 (0.8)	55 (4.9)	85 (4.1)	< 0.001
Neurologically favorable outcome, n (%)	188 (1.3)	37 (1.3)	27 (1.9)	2 (0.2)	17 (1.5)	37 (1.8)	< 0.001

\* *P* values are calculated to test the homogeneity among the 5 cause groups.

ROSC indicates return of spontaneous circulation.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

**Table 5** Outcomes after out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Prehospital ROSC, n (%)	463 (17.3)	144 (7.2)	22 (1.7)	36 (3.4)	28 (3.7)	4 (2.1)	6 (2.3)	< 0.001
Total ROSC, n (%)	1003 (37.6)	1500 (75.0)	1213 (93.3)	894 (84.2)	637 (83.3)	143 (76.5)	211 (82.4)	< 0.001
Hospital admission, n (%)	1529 (57.3)	453 (22.7)	62 (4.8)	147 (13.8)	92 (12.0)	40 (21.4)	33 (12.9)	< 0.001
One-month survival, n (%)	382 (14.3)	84 (4.2)	9 (0.7)	12 (1.1)	12 (1.6)	7 (3.7)	4 (1.6)	< 0.001
Neurologically favorable outcome, n (%)	71 (2.7)	17 (0.9)	1 (0.1)	4 (0.4)	6 (0.8)	4 (2.1)	2 (0.8)	< 0.001

\**P* values are calculated to test the homogeneity among the 7 cause groups.  
ROSC indicates return of spontaneous circulation.

For peer review only

**Table 6** Factors associated with outcomes after out-of-Hospital cardiac arrests with non-cardiac origin

	One-month survival		Neurologically favorable outcome	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Adults (versus elderly)	0.75 (0.64-0.88)	0.99 (0.84-1.16)	1.09 (0.81-1.46)	0.91 (0.67-1.24)
Men	0.95 (0.82-1.10)	1.36 (1.12-1.65)	1.02 (0.76-1.37)	1.52 (1.07-2.15)
Witnessed by bystanders	4.41 (3.74-5.19)	4.13 (3.35-5.09)	4.48 (3.23-6.21)	4.83 (3.21-7.29)
Good activities of daily living	0.93 (0.80-1.08)	1.23 (1.03-1.47)	1.39 (1.02-1.88)	1.43 (1.02-2.02)
VF	2.74 (1.96-3.82)	2.04 (1.42-2.92)	7.72 (5.05-11.79)	5.40 (3.40-8.59)
Type of bystander CPR				
No CPR	Reference	Reference	Reference	Reference
Chest compression-only CPR	0.97 (0.81-1.16)	0.80 (0.66-0.98)	0.95 (0.67-1.35)	0.92 (0.64-1.33)
Conventional CPR with rescue breathing	1.47 (1.20-1.79)	1.07 (0.86-1.34)	1.01 (0.65-1.55)	0.89 (0.56-1.42)
Type of non-cardiac origin				
Respiratory diseases	0.42 (0.33-0.53)	0.51 (0.40-0.65)	0.70 (0.44-1.09)	0.76 (0.48-1.21)
Malignant tumors	0.05 (0.03-0.09)	0.06 (0.03-0.11)	0.06 (0.01-0.23)	0.06 (0.01-0.23)
Cerebrovascular diseases	0.31 (0.23-0.42)	0.27 (0.20-0.38)	0.57 (0.33-0.97)	0.34 (0.19-0.61)
Asphyxia	Reference	Reference	Reference	Reference
Hanging	0.26 (0.21-0.34)	0.56 (0.41-0.77)	0.31 (0.18-0.53)	0.55 (0.28-1.07)
Fall	0.04 (0.02-0.08)	0.03 (0.01-0.06)	0.03 (0.004-0.20)	0.01 (0.002-0.11)
Drowning	0.07 (0.04-0.12)	0.16 (0.09-0.29)	0.14 (0.05-0.38)	0.31 (0.11-0.90)
Traffic injury	0.10 (0.05-0.17)	0.05 (0.03-0.10)	0.29 (0.13-0.67)	0.10 (0.04-0.26)
Drug overdose	0.23 (0.11-0.50)	0.58 (0.26-1.29)	0.80 (0.29-2.21)	1.74 (0.58-5.19)
Others	0.26 (0.20-0.33)	0.29 (0.22-0.38)	0.67 (0.45-1.00)	0.60 (0.39-0.92)
Unclassified	0.10 (0.04-0.26)	0.10 (0.04-0.28)	0.29 (0.07-1.18)	0.27 (0.06-1.16)
Location of arrest				
Homes	Reference	Reference	Reference	Reference
Public places	0.78 (0.61-0.99)	1.45 (1.10-1.91)	1.11 (0.75-1.65)	1.54 (0.97-2.44)
Workplaces	1.29 (0.83-1.98)	1.40 (0.87-2.23)	1.26 (0.55-2.89)	0.95 (0.39-2.30)
Health care facilities	1.69 (1.38-2.07)	0.88 (0.69-1.12)	0.72 (0.42-1.24)	0.47 (0.26-0.85)
Others	0.70 (0.51-0.94)	1.67 (1.19-2.35)	0.68 (0.38-1.24)	1.35 (0.72-2.54)
Intravascular fluid	1.78 (1.50-2.11)	1.45 (1.14-1.84)	1.34 (0.94-1.91)	1.52 (0.97-2.38)
Intubation	1.62 (1.37-1.92)	1.02 (0.84-1.23)	0.73 (0.48-1.10)	0.50 (0.32-0.77)
Epinephrine	2.32 (1.87-2.88)	0.97 (0.71-1.32)	1.25 (0.74-2.09)	0.60 (0.31-1.17)
EMS response time (for one-increment of minute)	0.93 (0.91-0.96)	0.92 (0.90-0.95)	0.91 (0.86-0.96)	0.90 (0.84-0.95)
Year (for one-increment of year)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.02 (0.95-1.09)	1.05 (0.97-1.13)

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Epidemiology and outcome of out-of-hospital cardiac arrest with non-cardiac origin in Osaka: a population-based study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-006462.R1
Article Type:	Research
Date Submitted by the Author:	14-Oct-2014
Complete List of Authors:	Kitamura, Tetsuhisa; Osaka University, Graduate School of Medicine Kiyohara, Kosuke; Tokyo Women's Medical University, Sakai, Tomohiko; Osaka University, Department of Traumatology and Acute Critical Medicine Iwami, Taku ; Kyoto University , Health Service Nishiyama, Chika; Kyoto University, Department of Critical Care Nursing Kajino, Kentaro; Osaka National Hospital, Traumatology and Critical Care Medical Center Nishiuchi, Tatsuya; Kinki University, Department of Acute Medicine Hayashi, Yasuyuki; Osaka Saiseikai Senri Hospital, Senri Critical Care Medical Center Katayama, Yusuke; Osaka University, Department of Traumatology and Acute Critical Medicine Yoshiya, Kazuhisa; Osaka University, Department of Traumatology and Acute Critical Medicine Shimazu, Takeshi; Osaka University, Department of Traumatology and Acute Critical Medicine
<b>Primary Subject Heading</b>:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Cardiovascular medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

SCHOLARONE™  
Manuscripts

1 **Epidemiology and outcome of out-of-hospital cardiac arrest with**  
2 **non-cardiac origin in Osaka: a population-based study**

3  
4 Tetsuhisa Kitamura,<sup>1</sup> Kosuke Kiyohara,<sup>2</sup> Tomohiko Sakai,<sup>3</sup> Taku Iwami,<sup>4</sup> Chika Nishiyama,<sup>5</sup>  
5 Kentaro Kajino,<sup>6</sup> Tatsuya Nishiuchi,<sup>7</sup> Yasuyuki Hayashi,<sup>8</sup> Yusuke Katayama,<sup>3</sup> Kazuhisa  
6 Yoshiya,<sup>3</sup> Takeshi Shimazu<sup>3</sup>

7  
8 **Author affiliations**

9 <sup>1</sup>Division of Environmental Medicine and Population Sciences, Department of Social and  
10 Environmental Medicine, Graduate School of Medicine, Osaka University, Japan

11 <sup>2</sup>Department of Public Health, Tokyo Women's Medical University, Japan

12 <sup>3</sup>Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School  
13 of Medicine, Japan

14 <sup>4</sup>Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto, Japan

15 <sup>5</sup>Department of Critical Care Nursing, Graduate School of Medicine and School of Health  
16 Sciences, Kyoto University, Japan

17 <sup>6</sup>Traumatology and Critical Care Medical Center, National Hospital Organization Osaka  
18 National Hospital, Japan

1  
2  
3  
4  
5  
6 1 <sup>7</sup>Department of Acute Medicine, Kinki University Faculty of Medicine, Japan  
7

8  
9 2 <sup>8</sup>Senri Critical Care Medical Center, Osaka Saiseikai Senri Hospital, Japan  
10

11  
12 3

13  
14 4 **Correspondence to**

15  
16 5 Taku Iwami MD, PhD

17  
18  
19  
20 6 Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501  
21

22  
23 7 Phone: +81-75-753-2426; Fax: +81-75-753-2424  
24

25  
26 8 E-mail: iwamit@e-mail.jp  
27

28  
29 9  
30

31  
32 10 **Total word count:** 2848 words (main text). **Abstract:** 276 words.  
33

34  
35 11  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3  
4  
5  
6 **1 ABSTRACT**  
7

8  
9 **2 Objectives:** To evaluate epidemiological characteristics of out-of-hospital cardiac  
10  
11  
12 **3 arrests (OHCAs)** by detailed non-cardiac cause and factors associated with the  
13  
14  
15 **4 outcomes** after OHCAs with non-cardiac origin.  
16

17  
18 **5 Design:** A prospective, population-based observational study.  
19

20  
21 **6 Setting:** The Utstein Osaka Project.  
22

23  
24 **7 Participants:** 14,164 adult patients with OHCAs due to non-cardiac origin who were  
25  
26  
27 **8 resuscitated** by emergency-medical-service personnel or bystanders, and then were  
28  
29  
30 **9 transported** to medical institutions from January 2005 to December 2011.  
31

32  
33 **10 Primary outcome measures:** One-month survival after OHCA. Multiple logistic  
34  
35  
36 **11 regression analysis** was used to assess factors that were potentially associated with the  
37  
38  
39 **12 outcome.**

40  
41 **13 Results:** During the study period, the one-month survival rate was 5.3% (755/14,164).  
42  
43  
44 **14 The proportion** of one-month survival was 6.2% (510/8239) in external causes, 6.5%  
45  
46  
47 **15 (94/1148)** in respiratory diseases, 0.8% (11/1309) in malignant tumors, 4.9% (55/1114)  
48  
49  
50 **16 in strokes,** and 4.1% (85/2054) in others. As for external causes, the proportion of  
51  
52  
53 **17 one-month survival** was 14.3% (382/2670) in asphyxia, 4.2% (84/1999) in hanging,  
54  
55  
56 **18 0.7% (9/1300)** in fall, 1.1% (12/1062) in drowning, 1.6% (12/765) in traffic injury,  
57  
58  
59  
60

1 3.7% (7/187) in drug overuse, and 1.6% (4/256) in unclassified external causes. In a  
2 multivariate analysis, arrests witnessed by bystanders, good activities of daily living  
3 before arrests, ventricular fibrillation arrests, public places, intravenous fluid, and early  
4 emergency-medical-service response time were significant predictors for one-month  
5 outcome after OHCA with cardiac origin. The proportion of one-month survival of the  
6 whole OHCA with non-cardiac origin did not significantly increase (from 4.3%  
7 [86/2023] in 2005 to 4.9% [105/2126] in 2011) and the adjusted odds ratio for  
8 one-increment of year was 1.01 (95% confidence interval 0.97-1.06).

9 **Conclusions:** From a large OHCA registry in Osaka, we demonstrated that one-month  
10 survival after OHCA with non-cardiac origin was poor and stable.

11

1  
2  
3  
4  
5  
6 **1 Strengths and limitations of this study**  
7

8  
9 ■ This study showed that one-month survival after OHCA with non-cardiac origin  
10  
11 was poor and the survival trends did not improve year-by-year in Osaka during the  
12  
13 study period from 2005 to 2011. In addition, the survival rates differed by  
14  
15 detailed non-cardiac origin.  
16  
17  
18

19  
20 ■ The category of presumed non-cardiac causes is made clinically, as per the  
21  
22 Utstein-style international guidelines for cardiac arrest data reporting.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 INTRODUCTION

2 Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the  
3 industrialized world.<sup>1-4</sup> Although improvements in the chain of survival including the  
4 development of a public-access defibrillation system and revisions to cardiopulmonary  
5 resuscitation (CPR) guidelines have led to increased survival after OHCA with cardiac  
6 origin in some communities,<sup>5-7</sup> the outcome after OHCA with non-cardiac origin  
7 remains generally poor.<sup>7-13</sup>

8 Importantly, 20% to 40% of adult OHCA were reportedly of non-cardiac origin.<sup>7-13</sup>  
9 However, epidemiological characteristics of OHCA with non-cardiac origin have not  
10 been sufficiently investigated as much as those of OHCA with cardiac origin.  
11 Therefore, the evaluation of characteristics, trends, and outcomes by detailed  
12 non-cardiac cause and understanding the factors associated with the outcomes are  
13 needed to improve the survival after OHCA with non-cardiac origin.

14 The Utstein Osaka Project is a large prospective population-based cohort study of  
15 OHCA in Osaka, Japan, covering about 8.8 million residents.<sup>5</sup> During the 7 years from  
16 2005 to 2011, we enrolled approximately 14,000 OHCA with non-cardiac origin  
17 before emergency-medical-service (EMS) arrival. The present study aimed to evaluate  
18 the epidemiological characteristics of OHCA by detailed non-cardiac cause. In

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 addition, we evaluated factors associated with the outcomes after OHCA with  
2 non-cardiac origin in a multivariate analysis.  
3

For peer review only

## 1 METHODS

### 2 Study design and setting

3 The Utstein Osaka Project is a prospective, population-based registry of OHCA that is  
4 based on the standardized Utstein style.<sup>14,15</sup> This study enrolled adult patients aged  
5 =>20 years suffering OHCAs with non-cardiac origin before EMS arrival, who were  
6 resuscitated by EMS personnel or bystanders, and were transported to medical  
7 institutions in Osaka Prefecture from January 1, 2005 to December 31, 2011. In this  
8 study, we excluded pediatric OHCA patients because characteristics and outcomes  
9 from OHCAs differed between children and adults.<sup>16,17</sup>

10 Cardiac arrest was defined as the cessation of cardiac mechanical activity as  
11 confirmed by the absence of signs of circulation.<sup>14,15</sup> In this study, the arrests were  
12 classified into those of presumed cardiac origin and non-cardiac origin, the latter  
13 resulting from external causes, respiratory diseases, malignant tumors, strokes, and any  
14 other non-cardiac causes based on hospital medical records. Furthermore, external  
15 causes were divided into the seven categories: asphyxia, hanging, fall, drowning,  
16 traffic injury, drug overuse, and unclassified external causes. These diagnoses were  
17 made clinically by the physician in charge, working in collaboration with the EMS  
18 personnel.

1

## 2 EMS organization in Osaka

3 Details of the EMS system in Osaka were described previously.<sup>5</sup> Osaka is the second  
4 largest prefecture in Japan with a population of approximately 8.8 million inhabitants  
5 in an area of 1892 km<sup>2</sup>. In Osaka, there are 34 fire stations with emergency dispatch  
6 centers. The EMS system is operated by the local fire stations. When called, an  
7 ambulance is dispatched from the nearest fire station. Emergency services are provided  
8 24 hours each day by them, which is single-tiered in 32 stations and two-tiered in two  
9 stations. The latter uses medics followed by physicians.

10 Most highly-trained prehospital emergency care providers are called Emergency  
11 Life-Saving Technicians (ELSTs). Usually, each ambulance has a crew of three  
12 emergency providers including at least one ELST. They were allowed to insert an  
13 intravenous line and an adjunct airway, and to use a semi-automated external  
14 defibrillator for OHCA patients. Specially trained ELSTs were permitted to tracheal  
15 intubation since July 2004 and administer intravenous epinephrine since April 2006.

16 Do-not-resuscitate (DNR) orders or living wills are not generally accepted in Japan.  
17 EMS providers are not permitted to terminate resuscitation in the field. Therefore,  
18 almost patients with OHCA who were treated by EMS personnel were transported to a

1 hospital and enrolled in the Utstein Osaka Project, excluding those with decapitation,  
2 incineration, decomposition, rigor mortis, or dependent cyanosis.

#### 4 **CPR and AED training for the general public**

5 The use of an automated external defibrillator (AED) by citizens was permitted legally  
6 in July 2004. In Osaka, approximately 14,000 citizens per year participated in the CPR  
7 training programs, consisting of conventional CPR including chest compressions,  
8 mouth-to-mouth ventilation, and AED usage by local fire departments, the Japan Red  
9 Cross, Inc., and the Osaka Life Support Association.<sup>5</sup> All EMS providers perform CPR  
10 according to the Japanese CPR guidelines.<sup>4</sup>

#### 12 **Data collection and quality control**

13 Data collection were prospectively conducted using a form that included data  
14 recommended in the Utstein-style reporting guidelines for cardiac arrests.<sup>14,15</sup> These  
15 data included gender, age, first documented cardiac rhythm, witness status, location of  
16 arrests, activity of daily living (ADL) before arrests, time-courses of resuscitation, type  
17 of bystander-initiated CPR, public-access AED use, intravascular fluid, tracheal  
18 intubation, and intravascular epinephrine as well as prehospital return of spontaneous



1  
2  
3  
4  
5  
6 1 circulation (ROSC), total ROSC, one-month survival, and neurological status one  
7  
8  
9 2 month after the event. First documented rhythm was recorded and diagnosed by the  
10  
11  
12 3 EMS personnel with semi-automated defibrillators on the scene, and confirmed by the  
13  
14  
15 4 physician who was responsible for the on-line medical direction. Bystander CPR  
16  
17  
18 5 included chest compression-only CPR and conventional CPR with rescue breathing. A  
19  
20  
21 6 series of EMS times of call receipt, vehicle arrival at the scene, contact with patients,  
22  
23  
24 7 initiation of CPR, defibrillation by EMS, and hospital arrival were recorded  
25  
26  
27 8 automatically at the dispatch center.

28  
29 9 The data form was completed by the EMS personnel in cooperation with the  
30  
31  
32 10 physicians in charge of the patients, and the data were integrated into the registry  
33  
34  
35 11 system on the Information Center for Emergency Medical Services of Osaka, and then  
36  
37  
38 12 checked by the investigators. If the data sheet was incomplete, the relevant EMS  
39  
40  
41 13 personnel were contacted and questioned for data completion.

42  
43  
44 14 All survivors suffering OHCA were followed up for up to one-month after the event  
45  
46  
47 15 by the EMS personnel in charge. One-month neurological outcomes were determined  
48  
49  
50 16 by the physician responsible for treating the patient, using the cerebral performance  
51  
52  
53 17 category (CPC) scale: category 1, good cerebral performance; category 2, moderate  
54  
55  
56 18 cerebral disability; category 3, severe cerebral disability; category 4, coma or  
57  
58  
59  
60

1 vegetative state; and category 5, death.<sup>14,15</sup>

2

### 3 **Outcome measures**

4 The main outcome measure was one-month survival. Secondary outcome measures  
5 included prehospital and total ROSCs, admission to hospital, and one-month survival  
6 with neurologically favorable outcome. Neurologically favorable outcome was defined  
7 as CPC category 1 or 2.<sup>14,15</sup>

8

### 9 **Statistical analysis**

10 In this study, patient and EMS characteristics of OHCAs with non-cardiac origin and  
11 their outcomes were compared between the groups using unpaired analysis of variance  
12 for numerical variables, and chi-square test or Fisher's exact test for categorical  
13 variables by cause of arrest. First, non-cardiac causes were divided into the following  
14 five groups; external causes, respiratory diseases, malignant tumors, strokes, and any  
15 other non-cardiac causes. Next, external causes were further divided into asphyxia,  
16 hanging, fall, drowning, traffic injury, drug overuse, and unclassified external causes.  
17 Age-adjusted annual incidence of OHCAs by non-cardiac origin was calculated by the  
18 direct method using 2005 census data and 1985 Japanese model population.<sup>18,19</sup>

1  
2  
3  
4  
5  
6 1 Poisson regression models for the trends in the incidence and one-month survival rate  
7  
8  
9 2 were used. Multiple logistic regression analysis assessed the factors associated with  
10  
11  
12 3 one-month survival and neurological favorable outcome, and adjusted odds ratios  
13  
14 4 (AORs) and their 95% confidence intervals (CIs) were calculated. As potential  
15  
16  
17 5 confounders, factors that were biologically essential and considered to be associated  
18  
19  
20 6 with clinical outcomes were taken in the multivariable analyses.<sup>7</sup> These variables  
21  
22  
23 7 included age (20-64, ≥65 years old), gender (men, women), witness status (none,  
24  
25  
26 8 witnessed by bystanders), ADL before arrests (good, other), first documented rhythm  
27  
28  
29 9 (VF, non-VF), bystander CPR status (none, compression-only CPR, conventional CPR),  
30  
31  
32 10 type of non-cardiac causes (the 11 categories described above), location of arrests  
33  
34  
35 11 (homes, public places, work places, health care facilities, others), intravascular fluid  
36  
37  
38 12 (yes, no), intubation (yes, no), epinephrine (yes, no), EMS response time (call to  
39  
40  
41 13 contact with patients), and year of arrest. In addition, we conducted a multivariate  
42  
43  
44 14 analysis of one-month survival from OHCA with non-cardiac origin after dividing the  
45  
46  
47 15 two groups: internal (respiratory diseases, malignant tumors, and strokes) and external  
48  
49  
50 16 (asphyxia, hanging, fall, drowning, traffic injury, and drug overuse) causes.

51  
52 17 All statistical analyses were performed using the SPSS statistical package ver21.0J  
53  
54  
55 18 (IBM Corp. Armonk, NY). All of the tests were 2-tailed and *P* values of <0.05 were  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 considered statistically significant.  
7  
8  
9 2  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## 1 RESULTS

2 Figure 1 shows an overview of the study patients based on the Utstein template. A total  
3 of 47,735 adult arrests were documented during these seven years. Resuscitation was  
4 attempted in 43,845, and 15,505 of them were of non-cardiac origin. Excluding 1341  
5 victims who were witnessed by EMS (arrests after EMS arrival), 14,164 (5561 in  
6 bystander-witnessed cases and 8603 in non-witnessed cases) were eligible for our  
7 analyses. Among these arrests, 8239 (58.2%) were due to external causes, 1448  
8 (10.2%) respiratory diseases, 1309 (9.2%) malignant tumors, 1114 (7.9%) strokes, and  
9 2054 (14.5%) others. Among external causes, 2670 (16.5%) were of asphyxia, 1999  
10 (14.1%) hanging, 1300 (9.2%) fall, 1062 (7.5%) drowning, 765 (5.4%) traffic injury,  
11 and 256 (1.8%) unclassified external cause.

12 The age-adjusted annual incidence rates per 100,000 persons by non-cardiac cause  
13 were calculated over time (Table 1). The incidence rate of OHCA with external  
14 causes significantly increased from 12.4 in 2005 to 13.3 in 2011 (P for trend=0.024).  
15 The incidence rate significantly decreased among OHCA patients with respiratory  
16 diseases (from 2.2 in 2005 to 1.6 in 2011, P for trend=0.018) and strokes (from 2.0 in  
17 2005 to 1.3 in 2011, P for trend<0.001). The unadjusted one-month survival rates by  
18 non-cardiac cause were almost stable during the study period.

1 Patient and EMS characteristics of OHCAs with non-cardiac origin according to the  
2 cause are shown in Table 2, and their outcomes in Table 4. The mean age of all OHCA  
3 patients with non-cardiac origin was 66.8 years and males were 58.0%. The proportion  
4 of bystander-witnessed arrests, ADL before arrests, first documented rhythm, type of  
5 bystander CPR, and advanced life supports such as intravascular fluid, intubation, and  
6 epinephrine exceedingly varied between the five groups. In the whole patients, the rate  
7 of one-month survival and neurologically favorable outcome was 5.3% and 1.3%. The  
8 proportion of one-month survival was 6.2% in external causes, 6.5% in respiratory  
9 diseases, 0.8% in malignant tumors, 4.9% in strokes, and 4.1% in others. Furthermore,  
10 patient and EMS characteristics of OHCAs in external causes are shown in Table 3,  
11 and their outcomes in Table 5. The characteristics and outcomes varied between the  
12 seven groups. The proportion of one-month survival was 14.3% in asphyxia, 4.2% in  
13 hanging, 0.7% in fall, 1.1% in submersion, 1.6% in traffic injury, 3.7% in drug overuse,  
14 and 1.6% in unclassified external cause. The proportion of bystander chest  
15 compression-only CPR and conventional CPR with rescue breathing was 23.2% and  
16 13.1% in whole OHCAs with non-cardiac origin, and 22.1% and 14.3% in  
17 bystander-witnessed OHCAs.

18 Table 6 shows factors contributing to one-month survival and neurologically

1  
2  
3  
4  
5  
6 1 favorable outcome after OHCAs with non-cardiac origin. In one-month survival,  
7  
8  
9 2 arrests witnessed by bystanders (AOR 4.13, 95% CI 3.35-5.09), good ADL before  
10  
11  
12 3 arrests (AOR 1.23, 95% CI 1.03-1.47), VF as first documented rhythm (AOR 2.04,  
13  
14 4 95% CI 1.42-2.92), public places (AOR 1.45, 95% CI 1.10-1.91), intravenous fluid  
15  
16  
17 5 (AOR 1.45, 95% CI 1.14-1.84), and early EMS response time (AOR for one-increment  
18  
19  
20 6 of minute 0.92, 95% CI 0.90-.095) were associated with improving outcome. However,  
21  
22  
23 7 type of bystander CPR, intubation, and epinephrine were not associated with better  
24  
25  
26 8 outcome. Compared with asphyxia, the AORs were significantly lower in respiratory  
27  
28  
29 9 diseases (0.51, 95% CI 0.40-0.65), malignant tumors (0.06, 95% CI 0.03-0.11), stroke  
30  
31  
32 10 (0.27, 95% CI 0.20-0.38), hanging (0.56, 95% CI 0.41-0.77), fall (0.03, 95% CI  
33  
34  
35 11 0.01-0.06), drowning (0.16, 95% CI 0.09-0.29), and traffic injury (0.05, 95% CI  
36  
37  
38 12 0.03-0.10). The proportion of one-month survival of the whole OHCAs with  
39  
40  
41 13 non-cardiac origin did not significantly increase (from 4.3% [86/2023] in 2005 to 4.9%  
42  
43  
44 14 [105/2126] in 2011) and the AOR for one-increment of year was 1.01 (95% CI  
45  
46  
47 15 0.97-1.06). The AORs of neurologically favorable outcome after OHCAs with  
48  
49  
50 16 non-cardiac origin were almost similar to those of one-month survival.

51  
52 17 Subgroup analyses after dividing the two groups (internal and external causes) are  
53  
54  
55 18 shown in Supplemental Table. As for internal causes, arrests witnessed by bystanders  
56  
57  
58  
59  
60

1 (AOR 2.86, 95% CI 1.99-4.11), VF as first documented rhythm (AOR 2.35, 95% CI  
1.30-4.24), and public places (AOR 2.01, 95% CI 1.21-3.36) were associated with  
improving outcome. As for external causes, adults (AOR 1.51, 95% CI 1.17-1.96),  
arrests witnessed by bystanders (AOR 5.03, 95% CI 3.71-6.81), good ADL before  
arrests (AOR 1.34, 95% CI 1.08-1.67), intravenous fluid (AOR 1.69, 95% CI  
1.27-2.25), and early EMS response time (AOR for one-increment of minute 0.93, 95%  
CI 0.90-0.96) were associated with improving outcome.



1  
2  
3  
4  
5  
6 **1 DISCUSSION**  
7

8  
9 2 The extensive OHCA registry in Osaka showed that one-month survival after OHCA  
10  
11 3 with non-cardiac origin was poor and the survival trends did not improve year-by-year.

12  
13  
14 4 In addition, the survivals differed by detailed non-cardiac origin. To further improve  
15  
16 5 survival after OHCA, sufficient attention should be paid to the epidemiological  
17  
18 6 characteristics of OHCA with non-cardiac origin as much as those of OHCA with  
19  
20 7 cardiac origin, and this study describing the actual situation regarding the incidence  
21  
22 8 and outcome of OHCA with non-cardiac origin provides valuable information to  
23  
24 9 improve the survival.  
25  
26  
27  
28  
29  
30  
31

32 10 Our study observed that the outcomes of OHCA with non-cardiac origin were poor  
33  
34 11 and stable during the seven years. In a previous study in Japan, neurologically  
35  
36 12 favorable outcome of bystander-witnessed OHCA with non-cardiac origin increased  
37  
38 13 from 2005 to 2011, but the absolute survival was very low,<sup>7</sup> and this result was similar  
39  
40 14 with ours. Improving the outcome of OHCA with non-cardiac origin poses an  
41  
42 15 important problem in resuscitation science because 20~40% of adult OHCA are of  
43  
44 16 non-cardiac origin.<sup>7-13</sup> In addition, the survivals exceedingly differed by detailed  
45  
46 17 non-cardiac origin, which also suggests the need and importance of an origin-specific  
47  
48 18 strategy for improving the outcomes.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 We also showed that the OHCA incidence trends differed by detailed non-cardiac  
2 origin. For instance, the incidence rate of OHCA due to strokes significantly  
3 decreased during the study period. Although the reasons for the decrement were  
4 unclear, better blood pressure control and decreasing smoking rate in recent years of  
5 Japan might be one of the possible explanations for this phenomenon.<sup>20</sup> In fact, the  
6 numbers of stroke patients in Japan has also been decreasing.<sup>21</sup> On the other hand, the  
7 incidence rates of OHCA with external causes increased and the outcomes after  
8 OHCA with external causes excluding asphyxia were miserable. For example,  
9 external OHCA due to trauma, drug overdose, or hanging in metropolitan area of  
10 Australia were more common and the survivals from traumatic and hanging-associated  
11 OHCA were not always futile. Therefore, there were regional variations on the  
12 incidence and outcome from OHCA with external causes,<sup>22,23</sup> and the  
13 countermeasures would differ by regions. However, most importantly, more efforts  
14 should focus on prevention of OHCA with external causes because many of them are  
15 preventable.<sup>1-4</sup>

16 In a multivariable analysis, intravenous fluid administration was associated with  
17 better one-month survival after OHCA with non-cardiac origin. In preceding studies,  
18 prehospital intravenous fluid for OHCA including both cardiac and non-cardiac

1 origins was not associated with the improved outcome,<sup>24</sup> whereas intravenous access  
2 were associated with a reduction in hospital mortality among non-injured, non-cardiac  
3 arrest patients<sup>25</sup> Thus, the effects of fluid administration on prehospital emergency  
4 patients were under debate, and further investigations by other cohorts or randomized  
5 controlled trials are needed to confirm these associations.

6 In this study, a multivariate analysis also underscored that either bystander-initiated  
7 chest compression-only CPR or conventional CPR with rescue breathing was not  
8 effective for OHCA with non-cardiac origin. From a nationwide study focused on  
9 43,000 bystander-witnessed OHCA with non-cardiac origin, we demonstrated that  
10 conventional CPR with rescue breathing had an incremental benefit for OHCA with  
11 non-cardiac origin, but the impact on the overall survival after OHCA was small.<sup>8</sup>  
12 Considering these results, the effectiveness of bystander CPR on OHCA with  
13 non-cardiac origin might be limited. In addition, attempted resuscitation rates in our  
14 area was exceedingly higher at 92% compared with those in western countries,<sup>22,26</sup>  
15 which might be also one of the possible explanations for the lack of impact of  
16 bystander CPR in our multivariate model. However, as recommended in the CPR  
17 guidelines,<sup>1-4</sup> bystander CPR plays a key role in the “chain of survival” and increasing  
18 the proportion of bystander CPR for OHCA patients is important.

1  
2  
3  
4  
5  
6 1 Furthermore, factors such as arrests witnessed by bystanders and earlier EMS  
7  
8  
9 2 response time were also independent predictors of better outcome after OHCA with  
10  
11  
12 3 non-cardiac origin in a multivariate analysis. This would indicate the importance of an  
13  
14 4 early EMS activation in the chain of survival<sup>1-4</sup> and suggests that activating the EMS  
15  
16  
17 5 system quickly leads to improving the outcomes after OHCA with non-cardiac origin.  
18  
19  
20 6 In addition, the verification of the effects on prehospital emergency care as well as  
21  
22  
23 7 in-hospital treatment is essential to improve survival after OHCA with non-cardiac  
24  
25  
26 8 origin.

27  
28  
29 9 The present study has some inherent limitations. First, the category of presumed  
30  
31  
32 10 cardiac or non-cardiac causes is made clinically, as per the Utstein-style international  
33  
34  
35 11 guidelines for cardiac arrest data reporting.<sup>14,15</sup> Second, information on post-arrest care  
36  
37  
38 12 is lacking. In-hospital treatment (e.g., hemodynamic support, cardiovascular  
39  
40  
41 13 intervention, induced hypothermia) might affect survival after OHCA.<sup>27</sup> Third,  
42  
43  
44 14 unmeasured confounding factors may have influenced the association between OHCA  
45  
46  
47 15 with non-cardiac origin and the outcome.

48  
49  
50 16

## 51 52 17 **CONCLUSION**

53  
54  
55 18 The large OHCA registry in Osaka demonstrated that one-month survival after OHCA  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 with non-cardiac origin was poor, the survival trends did not improve year-by-year, and  
2 the survivals differed by detailed non-cardiac origin. Further monitoring and discussion  
3 for epidemiology and outcome of OHCA with non-cardiac origin are warranted to  
4 improve survival after OHCA in this group.

5

For peer review only

1  
2  
3  
4  
5  
6 **1 Acknowledgments**  
7

8  
9 2 We are deeply indebted to all of the EMS personnel and concerned physicians in Osaka  
10  
11 3 Prefecture, and the Osaka Medical Association for their indispensable cooperation and  
12  
13 4 generous support. We also thank all members of the Utstein Osaka Project for their  
14  
15 5 contribution in the organization, coordination, and oversight as the steering committee.  
16  
17  
18  
19  
20  
21  
22

23 **7 Contributors**  
24

25  
26 8 All authors (TK, KK, TS, TI, CN, KK, TN, YH, YK, KY, and TS) participated in the study  
27  
28 9 conception and design, acquisition of data, analysis and interpretation of data, drafting the  
29  
30 10 article and revising it critically for important intellectual content, and final approval of the  
31  
32 11 manuscript.  
33  
34  
35  
36  
37  
38  
39  
40

41 **13 Funding**  
42

43  
44 14 This study was supported by a scientific research grant from the Ministry of Health, Labour,  
45  
46 15 and Welfare of Japan (25112601).  
47  
48  
49  
50

51  
52 **17 Competing interests**  
53

54  
55 18 None.  
56  
57  
58  
59  
60

1

**2 Ethics approval**

3 The study was approved by the institutional review board of Osaka University with the assent  
4 of the EMS authorities of the local governments in Osaka Prefecture.

5

**6 Provenance and peer review**

7 Not commissioned; externally peer reviewed.

8

**9 Data sharing statement**

10 TK had full access to all of the data in the study and takes responsibility for the integrity of the  
11 data and the accuracy of the data analysis.

12

**13 Open Access**

14 This is an Open Access article distributed in accordance with the Creative Commons  
15 Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute,  
16 remix, adapt, build upon this work noncommercially, and license their derivative works on  
17 different terms, provided the original work is properly cited and the use is non-commercial.

18 See: <http://creativecommons.org/licenses/by-nc/3.0/>

19

1  
2  
3  
4  
5  
6 **1 REFERENCES**  
7

- 8  
9 2 1. 2010 International consensus on cardiopulmonary resuscitation and emergency  
10  
11 cardiovascular care science with treatment recommendations. *Circulation*  
12  
13 2010;122:S250-605.  
14  
15  
16  
17 5 2. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and  
18  
19 emergency cardiovascular care. *Circulation* 2010;122:S639-946.  
20  
21  
22  
23 7 3. European Resuscitation Council Guidelines for Resuscitation 2010. *Resuscitation*  
24  
25 2010;81:1219-451.  
26  
27  
28  
29 9 4. 2010 Japanese guidelines for emergency care and cardiopulmonary resuscitation. 1st ed.  
30  
31 Tokyo: Health Shuppansha; 2011 (in Japanese).  
32  
33  
34  
35 11 5. Iwami T, Nichol G, Hiraide A, *et al.* Continuous improvements of chain of survival  
36  
37 increased survival after out-of-hospital cardiac arrests: a large-scale population-based  
38  
39 study. *Circulation* 2009;119:728-34.  
40  
41  
42  
43 14 6. Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation  
44  
45 during out-of-hospital ventricular fibrillation arrest: survival implications of guideline  
46  
47 changes. *Circulation* 2006;114:2760-5.  
48  
49  
50  
51  
52 17 7. Kitamura T, Iwami T, Kawamura T, *et al.* Nationwide improvements in survival from  
53  
54 out-of-hospital cardiac arrests in Japan. *Circulation* 2012;126:2834-43.  
55  
56  
57  
58  
59  
60



- 1  
2  
3  
4  
5  
6 1 8. Kitamura T, Iwami T, Kawamura T, *et al.* Bystander-initiated rescue breathing for  
7  
8  
9 2 out-of-hospital cardiac arrests of non-cardiac origin. *Circulation* 2010;122:293-9.  
10  
11  
12 3 9. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin.  
13  
14 4 Epidemiology and outcome. *Eur Heart J* 1997;18:1122-8.  
15  
16  
17 5 10. Engdahl J, Bång A, Karlson BW, *et al.* Characteristics and outcome among patients  
18  
19 6 suffering from out of hospital cardiac arrest of non-cardiac aetiology. *Resuscitation*  
20  
21 7 2003;57:33-41.  
22  
23  
24  
25  
26 8 11. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital  
27  
28 9 cardiac arrest of non-cardiac origin. *Resuscitation* 2007;72:200-7.  
29  
30  
31  
32 10 12. Iwami T, Hiraide A, Nakanishi N, *et al.* Age and sex analyses of out-of-hospital cardiac  
33  
34 11 arrest in Osaka, Japan. *Resuscitation* 2003;57:145-52.  
35  
36  
37  
38 12 13. Engdahl J, Holmberg M, Karlson BW, *et al.* The epidemiology of out-of-hospital 'sudden'  
39  
40 13 cardiac arrest. *Resuscitation* 2002;52:235-45.  
41  
42  
43  
44 14 14. Cummins RO, Chamberlain DA, Abramson NS, *et al.* Recommended guideline for  
45  
46 15 uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style: a statement  
47  
48 16 for health professionals from a task force of the American Heart Association, the  
49  
50 17 European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the  
51  
52 18 Australian Resuscitation Council. *Circulation* 1991;84:960-75.  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 15. Jacobs I, Nadkarni V, Bahr J, *et al.* Cardiac arrest and cardiopulmonary resuscitation  
7  
8  
9 2 outcome reports: update and simplification of the Utstein templates for resuscitation  
10  
11 3 registries: a statement for healthcare professionals from a task force of the International  
12  
13 4 Liaison Committee on Resuscitation (American Heart Association, European  
14  
15 Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation  
16  
17 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
18  
19 Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.  
20  
21  
22  
23 7  
24  
25  
26 8 16. Nitta M, Iwami T, Kitamura T, *et al.* Age-specific differences in outcomes after  
27  
28 9 out-of-hospital cardiac arrests. *Pediatrics* 2011;128:e812-20.  
29  
30  
31  
32 10 17. Atkins DL, Everson-Stewart S, Sears GK, *et al.* Epidemiology and outcomes from  
33  
34 11 out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium  
35  
36 12 Epistry-Cardiac Arrest. *Circulation* 2009;119:1484-91.  
37  
38  
39  
40 13 18. 2010 Population Census of Japan.  
41  
42 14 [http://www.stat.go.jp/data/kokusei/2010/index.htm?utm\\_source=twitterfeed&utm\\_mediu](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter)  
43  
44 15 [m=twitter](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter) (Accessed August 05, 2014) (in Japanese).  
45  
46  
47  
48  
49 16 19. Vital Statistics of Japan 2005. Tokyo: Health and Welfare Statistics Association; 2007.  
50  
51  
52 17 20. Hata J, Ninomiya T, Hirakawa Y, *et al.* Secular trends in cardiovascular disease and its  
53  
54 18 risk factors in Japanese: half-century data from the Hisayama Study (1961-2009).  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 *Circulation* 2013;128:1198-205.  
7  
8  
9 2 21. 2011 Overview of Patient Survey. <http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/>  
10  
11  
12 3 (Accessed August 05, 2014) (in Japanese).  
13  
14 4 22. Deasy C, Bray J, Smith K, *et al.* Traumatic out-of-hospital cardiac arrests in Melbourne,  
15  
16  
17 5 Australia. *Resuscitation* 2012;83:465-70.  
18  
19  
20 6 23. Deasy C, Bray J, Smith K, *et al.* Hanging-associated out-of-hospital cardiac arrests in  
21  
22  
23 7 Melbourne, Australia. *Emerg Med J* 2013;30:38-42.  
24  
25  
26 8 24. Hagihara A, Hasegawa M, Abe T, *et al.* Prehospital lactated ringer's solution treatment  
27  
28  
29 9 and survival in out-of-hospital cardiac arrest: a prospective cohort analysis. *PLoS Med*  
30  
31  
32 10 2013;10:e1001394.  
33  
34  
35 11 25. Seymour CW, Cooke CR, Hebert PL, *et al.* Intravenous access during out-of-hospital  
36  
37  
38 12 emergency care of noninjured patients: a population-based outcome study. *Ann Emerg*  
39  
40  
41 13 *Med* 2012;59:296-303.  
42  
43  
44 14 26. Nichol G, Thomas E, Callaway CW, *et al.* Regional variation in out-of-hospital cardiac  
45  
46  
47 15 arrest incidence and outcome. *JAMA* 2008;300:1423-31.  
48  
49  
50 16 27. Neumar RW, Nolan JP, Adrie C, *et al.* Post-cardiac arrest syndrome: epidemiology,  
51  
52  
53 17 pathophysiology, treatment, and prognostication. A Scientific Statement from the  
54  
55  
56 18 International Liaison Committee on Resuscitation; the American Heart Association  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and  
7  
8  
9 2 Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the  
10  
11  
12 3 Council on Clinical Cardiology; the Council on Stroke. *Circulation* 2008;118:2452-8.  
13  
14  
15 4  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 **Figure Legends**

2 **Figure 1** Overview of EMS-treated cardiac arrests with an abridged Utstein template from  
3 January 1, 2005 to December 31, 2011. EMS, emergency medical service.

For peer review only

4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Table 1** Age-adjusted incidences and unadjusted one-month survival rate of out-of-hospital cardiac arrests with non-cardiac origin according to the cause over time

	2005	2006	2007	2008	2009	2010	2011	P for trend
Age-adjusted Incidence per 100,000 persons								
External causes	12.4	12.3	13.2	12.8	13.2	13.3	13.3	0.024
Asphyxia	2.7	3.0	2.8	3.4	3.1	2.9	2.9	0.726
Hanging	3.4	3.4	4.1	3.4	3.7	3.9	3.9	0.158
Fall	2.4	2.5	3.1	2.4	2.9	3.0	2.7	0.396
Drowning	1.2	1.1	1.2	1.4	1.2	1.3	1.6	0.065
Traffic injury	1.6	1.5	1.4	1.4	1.4	1.5	1.4	0.229
Drug overdose	0.5	0.4	0.2	0.4	0.4	0.4	0.3	0.304
Unclassified	0.5	0.5	0.4	0.3	0.5	0.4	0.5	0.447
Respiratory diseases	2.2	1.8	1.8	1.7	1.3	1.3	1.6	0.018
Malignant tumors	1.6	1.8	1.8	1.7	1.5	1.3	1.6	0.109
Strokes	2.0	1.8	1.8	1.6	1.4	1.2	1.3	< 0.001
Others	2.7	3.3	3.1	2.9	2.7	2.5	2.4	0.087
Unadjusted one-month survival, % (n/N)								
External causes	4.8 (53/1100)	6.8 (72/1059)	5.7 (66/1164)	7.2 (85/1184)	7.1 (86/1207)	6.1 (75/1225)	5.6 (73/1300)	0.736
Asphyxia	10.4 (35/337)	15.4 (53/344)	13.0 (44/338)	15.6 (67/430)	16.3 (66/406)	14.8 (58/393)	14.0 (59/422)	0.374
Hanging	4.6 (12/261)	4.7 (12/255)	5 (16/318)	4.8 (13/273)	4.9 (14/287)	3.3 (10/301)	2.3 (7/304)	0.101
Fall	0.6 (1/159)	0.6 (1/169)	0.9 (2/219)	1.2 (2/165)	0.0 (0/197)	0.5 (1/208)	1.1 (2/183)	NA
Drowning	1.3 (2/151)	3.3 (4/120)	0.0 (0/128)	1.3 (2/159)	2.1 (3/144)	0.7 (1/148)	0.0 (0/212)	NA
Traffic injury	0.9 (1/116)	1.0 (1/101)	1.8 (2/109)	0.9 (1/106)	1.9 (2/103)	1.7 (2/115)	2.6 (3/115)	0.027

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

Drug overdose	3.0 (1/33)	0.0 (0/29)	5.6 (1/18)	0.0 (0/25)	3.3 (1/30)	11.1 (3/27)	4.0 (1/25)	NA
Unclassified	2.3 (1/43)	2.4 (1/41)	2.9 (1/34)	0.0 (0/26)	0.0 (0/40)	0.0 (0/33)	2.6 (1/39)	NA
Respiratory diseases	6.4 (17/267)	3.9 (8/206)	8.0 (17/212)	9.8 (21/214)	6.7 (11/165)	4.7 (8/169)	5.6 (12/215)	0.875
Malignant tumors	0.5 (1/186)	0.5 (1/194)	1.0 (2/202)	1.0 (2/196)	0.0 (0/178)	2.5 (4/159)	0.5 (1/194)	NA
Strokes	3.6 (7/196)	6.1 (11/179)	4.5 (8/176)	3.2 (5/154)	4.9 (7/143)	6.0 (8/134)	6.8 (9/132)	0.241
Others	2.9 (8/277)	7.0 (22/314)	1.3 (4/308)	4.5 (14/311)	4.3 (12/278)	5.3 (15/281)	3.5 (10/285)	0.808

NA indicates not analyzed.

For peer review only

**Table 2** Patient and EMS characteristics of out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n=14,164)	External causes (n = 8239)	Respiratory diseases (n=1448)	Malignant tumors (n=1309)	Strokes (n=1114)	Others (n=2054)	<i>P</i> value*
Age, yr, mean (SD)	66.8 (19.0)	63.5 (20.5)	76.1 (14.2)	71.9 (12.0)	67.7 (14.7)	69.8 (17.6)	< 0.001
Age group, n (%)							< 0.001
Adults aged 20-64 years	5513 (38.9)	3826 (46.4)	229 (15.8)	345 (26.4)	447 (40.1)	666 (32.4)	
Elderly aged >=65 years	8651 (61.1)	4413 (53.6)	1219 (84.2)	964 (73.6)	667 (59.9)	1388 (67.6)	
Men, n (%)	8215 (58.0)	4789 (58.1)	844 (58.3)	881 (67.3)	559 (50.2)	1142 (55.6)	< 0.001
Arrests witnessed by bystanders, n (%)	5561 (39.3)	2952 (35.8)	682 (47.1)	639 (48.8)	493 (44.3)	795 (38.7)	< 0.001
Good activities of daily living, n (%)	8522 (60.2)	5213 (63.3)	653 (45.1)	443 (33.8)	896 (80.4)	1317 (64.1)	< 0.001
First documented rhythm, n (%)							< 0.001
VF	324 (2.3)	119 (1.4)	35 (2.4)	26 (2.0)	69 (6.2)	75 (3.7)	
PEA	3356 (23.7)	1853 (22.5)	394 (27.2)	262 (20.0)	329 (29.5)	518 (25.2)	
Asystole	10196 (72.0)	6124 (74.3)	983 (67.9)	1008 (77.0)	647 (58.1)	1434 (69.8)	
Others	288 (2.0)	143 (1.7)	36 (2.5)	13 (1.0)	69 (6.2)	27 (1.3)	
Location of arrest, n (%)							< 0.001
Homes	9010 (63.6)	4435 (53.8)	1098 (75.8)	1217 (93.0)	801 (71.9)	1459 (71.0)	
Public places	2035 (14.4)	1608 (19.5)	59 (4.1)	24 (1.8)	156 (14.0)	188 (9.2)	
Work places	346 (2.4)	223 (2.7)	7 (0.5)	4 (0.3)	48 (4.3)	64 (3.1)	
Health care facilities	1505 (10.6)	904 (11.0)	248 (17.1)	55 (4.2)	63 (5.7)	235 (11.4)	
Others	1268 (9.0)	1069 (13.0)	36 (2.5)	9 (0.7)	46 (4.1)	108 (5.3)	
Public-access AED use, n (%)	13 (0.1)	4 (0.05)	2 (0.1)	0 (0.0)	5 (0.4)	2 (0.1)	0.001
Type of Bystander CPR, n (%)							< 0.001
No CPR	9023 (63.7)	5383 (65.3)	836 (57.7)	889 (67.9)	633 (56.8)	1282 (62.4)	
Chest compression-only CPR	3288 (23.2)	1811 (22.0)	408 (28.2)	297 (22.7)	283 (25.4)	489 (23.8)	



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

Conventional CPR with rescue breathing	1853 (13.1)	1045 (12.7)	204 (14.1)	123 (9.4)	198 (17.8)	283 (13.8)	
Intravascular fluid, n (%)	2320 (16.4)	1458 (17.7)	202 (14.0)	113 (8.6)	230 (20.6)	317 (15.4)	< 0.001
Intubation, n (%)	2639 (18.6)	1364 (16.6)	338 (23.3)	242 (18.5)	257 (23.1)	438 (21.3)	< 0.001
Epinephrine, n (%)	987 (7.0)	572 (6.9)	88 (6.1)	49 (3.7)	125 (11.2)	153 (7.4)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.9 (4.1)	8.0 (4.6)	7.7 (3.0)	7.7 (2.7)	7.7 (2.8)	7.9 (3.8)	0.003
Call to CPR by EMS, min, mean (SD)	8.5 (4.5)	8.8 (5.1)	8.1 (3.1)	8.1 (2.8)	8.2 (2.9)	8.4 (4.2)	< 0.001
Call to hospital arrival, min, mean (SD)	28.2 (8.6)	28.4 (8.6)	27.3 (8.2)	28.0 (8.9)	28.2 (8.4)	28.1 (8.7)	0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 3** Patient and EMS characteristics of out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Age, yr, mean (SD)	77.9 (14.4)	55.6 (17.4)	47.4 (17.4)	73.1 (14.8)	52.6 (19.0)	49.9 (19.5)	58.1 (19.3)	< 0.001
Age group, n (%)								< 0.001
Adults aged 20-64 years	403 (15.1)	1136 (66.8)	1055 (81.2)	210 (19.8)	523 (68.4)	141 (75.4)	158 (61.7)	
Elderly aged ≥65 years	2267 (84.9)	663 (33.2)	245 (18.8)	852 (80.2)	242 (31.6)	46 (24.6)	98 (38.3)	
Men, n (%)	1345 (50.4)	1290 (64.5)	781 (60.1)	530 (49.9)	558 (72.9)	117 (62.6)	168 (65.6)	< 0.001
Arrests witnessed by bystanders, n (%)	1801 (67.5)	27 (1.4)	510 (39.2)	56 (5.3)	476 (62.2)	10 (5.3)	72 (28.1)	< 0.001
Good activities of daily living, n (%)	1099 (41.2)	1769 (88.5)	685 (52.7)	854 (80.4)	517 (67.6)	133 (71.1)	156 (60.9)	< 0.001
First documented rhythm, n (%)								< 0.001
VF	56 (2.1)	13 (0.7)	19 (1.5)	12 (1.1)	14 (1.8)	1 (0.5)	4 (1.6)	
PEA	960 (36.0)	198 (9.9)	274 (21.1)	72 (6.8)	259 (33.9)	20 (10.7)	70 (27.3)	
Asystole	1589 (59.5)	1775 (88.8)	985 (75.8)	970 (91.3)	469 (61.3)	160 (85.6)	176 (68.8)	
Others	65 (2.4)	13 (0.7)	22 (1.7)	8 (0.8)	23 (3.0)	6 (3.2)	6 (2.3)	
Location of arrest, n (%)								< 0.001
Homes	1596 (59.8)	1667 (83.4)	139 (10.7)	770 (72.5)	2 (0.3)	150 (80.2)	111 (43.4)	
Public places	139 (5.2)	86 (4.3)	553 (42.5)	83 (7.8)	677 (88.5)	14 (7.5)	56 (21.9)	
Workplaces	35 (1.3)	94 (4.7)	44 (3.4)	3 (0.3)	7 (0.9)	7 (3.7)	33 (12.9)	
Health care facilities	835 (31.3)	27 (1.4)	12 (0.9)	14 (1.3)	1 (0.1)	0 (0.0)	15 (5.9)	
Others	65 (2.4)	125 (6.3)	552 (42.5)	192 (18.1)	78 (10.2)	16 (8.6)	41 (16.0)	

1										
2										
3										
4										
5										
6										
7	Public-access AED use, n (%)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.214
8	Type of Bystander CPR, n (%)									< 0.001
9	No CPR	1386 (51.9)	1174 (58.7)	1191 (91.6)	608 (57.3)	673 (88.0)	154 (82.4)	197 (77.0)		
10	Chest compression-only CPR	748 (28.0)	549 (27.5)	93 (7.2)	281 (26.5)	74 (9.7)	23 (12.3)	43 (16.8)		
11	Conventional CPR with rescue									
12	breathing	536 (20.1)	276 (13.8)	16 (1.2)	173 (16.3)	18 (2.4)	10 (5.3)	16 (6.2)		
13	Intravascular fluid, n (%)	540 (20.2)	393 (19.7)	107 (8.2)	281 (26.5)	76 (9.9)	27 (14.4)	34 (13.3)		< 0.001
14	Intubation, n (%)	800 (30.0)	167 (8.4)	41 (3.2)	251 (23.6)	31 (4.1)	33 (17.6)	41 (16.0)		< 0.001
15	Epinephrine, n (%)	326 (12.2)	83 (4.2)	41 (3.2)	68 (6.4)	37 (4.8)	6 (3.2)	11 (4.3)		< 0.001
16	Call to contact with a patient by EMS (EMS									
17	response time), min, mean (SD)	7.6 (2.9)	7.8 (3.3)	7.4 (3.3)	9.4 (7.6)	7.6 (4.2)	14.2 (10.7)	9.4 (7.3)		< 0.001
18	Call to CPR by EMS personnel, min, mean									
19	(SD)	7.9 (3.1)	8.6 (3.9)	8.2 (3.8)	10.0 (7.5)	9.3 (5.9)	14.4 (10.0)	11.0 (8.7)		< 0.001
20	Call to hospital arrival, min, mean (SD)	28.6 (8.6)	28.2 (7.9)	27.5 (8.3)	29.1 (9.3)	27.1 (8.8)	32.1 (11.1)	29.5 (9.4)		< 0.001

\*P values are calculated to test the homogeneity among the 7 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 4** Outcomes after out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 1,4164)	External causes (n = 8239)	Respiratory diseases (n = 1448)	Malignant tumors (n = 1309)	Strokes (n = 1114)	Others (n =2054)	<i>P</i> value *
Prehospital ROSC, n (%)	1229 (8.7)	703 (8.5)	114 (7.9)	57 (4.4)	216 (19.4)	139 (6.8)	< 0.001
Total ROSC, n (%)	4744 (33.5)	2638 (32.0)	620 (42.8)	234 (17.9)	650 (58.3)	602 (29.3)	< 0.001
Hospital admission, n (%)	4142 (29.2)	2356 (28.6)	530 (36.6)	173 (13.2)	585 (52.5)	498 (24.2)	< 0.001
One-month survival, n (%)	755 (5.3)	510 (6.2)	94 (6.5)	11 (0.8)	55 (4.9)	85 (4.1)	< 0.001
Neurologically favorable outcome, n (%)	188 (1.3)	105 (1.3)	27 (1.9)	2 (0.2)	17 (1.5)	37 (1.8)	< 0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

ROSC indicates return of spontaneous circulation.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

**Table 5** Outcomes after out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value *
Prehospital ROSC, n (%)	463 (17.3)	144 (7.2)	22 (1.7)	36 (3.4)	28 (3.7)	4 (2.1)	6 (2.3)	< 0.001
Total ROSC, n (%)	1003 (37.6)	1500 (75.0)	1213 (93.3)	894 (84.2)	637 (83.3)	143 (76.5)	211 (82.4)	< 0.001
Hospital admission, n (%)	1529 (57.3)	453 (22.7)	62 (4.8)	147 (13.8)	92 (12.0)	40 (21.4)	33 (12.9)	< 0.001
One-month survival, n (%)	382 (14.3)	84 (4.2)	9 (0.7)	12 (1.1)	12 (1.6)	7 (3.7)	4 (1.6)	< 0.001
Neurologically favorable outcome, n (%)	71 (2.7)	17 (0.9)	1 (0.1)	4 (0.4)	6 (0.8)	4 (2.1)	2 (0.8)	< 0.001

\*P values are calculated to test the homogeneity among the 7 cause groups.

ROSC indicates return of spontaneous circulation.

**Table 6** Factors associated with outcomes after out-of-Hospital cardiac arrests with non-cardiac origin

	One-month survival				Neurologically favorable outcome			
	Crude OR	(95% CI)	Adjusted OR	(95% CI)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	0.95	(0.82-1.10)	1.36	(1.12-1.65)	1.02	(0.76-1.37)	1.52	(1.07-2.15)
Men	0.75	(0.64-0.88)	0.99	(0.84-1.16)	1.09	(0.81-1.46)	0.91	(0.67-1.24)
Witnessed by bystanders	4.41	(3.74-5.19)	4.13	(3.35-5.09)	4.48	(3.23-6.21)	4.83	(3.21-7.29)
Good activities of daily living	0.93	(0.80-1.08)	1.23	(1.03-1.47)	1.39	(1.02-1.88)	1.43	(1.02-2.02)
VF	2.74	(1.96-3.82)	2.04	(1.42-2.92)	7.72	(5.05-11.79)	5.40	(3.40-8.59)
Type of bystander CPR								
No CPR	Reference		Reference		Reference		Reference	
Chest compression-only CPR	0.97	(0.81-1.16)	0.80	(0.66-0.98)	0.95	(0.67-1.35)	0.92	(0.64-1.33)
Conventional CPR with rescue breathing	1.47	(1.20-1.79)	1.07	(0.86-1.34)	1.01	(0.65-1.55)	0.89	(0.56-1.42)
Type of non-cardiac origin								
Respiratory diseases	0.42	(0.33-0.53)	0.51	(0.40-0.65)	0.70	(0.44-1.09)	0.76	(0.48-1.21)
Malignant tumors	0.05	(0.03-0.09)	0.06	(0.03-0.11)	0.06	(0.01-0.23)	0.06	(0.01-0.23)
Strokes	0.31	(0.23-0.42)	0.27	(0.20-0.38)	0.57	(0.33-0.97)	0.34	(0.19-0.61)
Asphyxia	Reference		Reference		Reference		Reference	
Hanging	0.26	(0.21-0.34)	0.56	(0.41-0.77)	0.31	(0.18-0.53)	0.55	(0.28-1.07)
Fall	0.04	(0.02-0.08)	0.03	(0.01-0.06)	0.03	(0.004-0.20)	0.01	(0.002-0.11)
Drowning	0.07	(0.04-0.12)	0.16	(0.09-0.29)	0.14	(0.05-0.38)	0.31	(0.11-0.90)

1							
2							
3							
4							
5							
6							
7	Traffic injury	0.10 (0.05-0.17)	0.05 (0.03-0.10)	0.29 (0.13-0.67)	0.10 (0.04-0.26)		
8							
9	Drug overdose	0.23 (0.11-0.50)	0.58 (0.26-1.29)	0.80 (0.29-2.21)	1.74 (0.58-5.19)		
10							
11	Others	0.26 (0.20-0.33)	0.29 (0.22-0.38)	0.67 (0.45-1.00)	0.60 (0.39-0.92)		
12							
13	Unclassified	0.10 (0.04-0.26)	0.10 (0.04-0.28)	0.29 (0.07-1.18)	0.27 (0.06-1.16)		
14							
15	Location of arrest						
16							
17	Homes	Reference	Reference	Reference	Reference		
18							
19	Public places	0.78 (0.61-0.99)	1.45 (1.10-1.91)	1.11 (0.75-1.65)	1.54 (0.97-2.44)		
20							
21	Workplaces	1.29 (0.83-1.98)	1.40 (0.87-2.23)	1.26 (0.55-2.89)	0.95 (0.39-2.30)		
22							
23	Health care facilities	1.69 (1.38-2.07)	0.88 (0.69-1.12)	0.72 (0.42-1.24)	0.47 (0.26-0.85)		
24							
25	Others	0.70 (0.51-0.94)	1.67 (1.19-2.35)	0.68 (0.38-1.24)	1.35 (0.72-2.54)		
26							
27	Intravascular fluid	1.78 (1.50-2.11)	1.45 (1.14-1.84)	1.34 (0.94-1.91)	1.52 (0.97-2.38)		
28							
29	Intubation	1.62 (1.37-1.92)	1.02 (0.84-1.23)	0.73 (0.48-1.10)	0.50 (0.32-0.77)		
30							
31	Epinephrine	2.32 (1.87-2.88)	0.97 (0.71-1.32)	1.25 (0.74-2.09)	0.60 (0.31-1.17)		
32							
33	EMS response time (for one-increment of minute)	0.93 (0.91-0.96)	0.92 (0.90-0.95)	0.91 (0.86-0.96)	0.90 (0.84-0.95)		
34							
35	Year (for one-increment of year)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.02 (0.95-1.09)	1.05 (0.97-1.13)		

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

1 **Epidemiology and outcome of out-of-hospital cardiac arrest with**  
2 **non-cardiac origin in Osaka: a population-based study**

3  
4 Tetsuhisa Kitamura,<sup>1</sup> Kosuke Kiyohara,<sup>2</sup> Tomohiko Sakai,<sup>3</sup> Taku Iwami,<sup>4</sup> Chika Nishiyama,<sup>5</sup>  
5 Kentaro Kajino,<sup>6</sup> Tatsuya Nishiuchi,<sup>7</sup> Yasuyuki Hayashi,<sup>8</sup> Yusuke Katayama,<sup>3</sup> Kazuhisa  
6 Yoshiya,<sup>3</sup> Takeshi Shimazu<sup>3</sup>

7  
8 **Author affiliations**

9 <sup>1</sup>Division of Environmental Medicine and Population Sciences, Department of Social and  
10 Environmental Medicine, Graduate School of Medicine, Osaka University, Japan

11 <sup>2</sup>Department of Public Health, Tokyo Women's Medical University, Japan

12 <sup>3</sup>Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School  
13 of Medicine, Japan

14 <sup>4</sup>Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto, Japan

15 <sup>5</sup>Department of Critical Care Nursing, Graduate School of Medicine and School of Health  
16 Sciences, Kyoto University, Japan

17 <sup>6</sup>Traumatology and Critical Care Medical Center, National Hospital Organization Osaka  
18 National Hospital, Japan



1  
2  
3  
4  
5  
6 1 <sup>7</sup>Department of Acute Medicine, Kinki University Faculty of Medicine, Japan  
7  
8

9 2 <sup>8</sup>Senri Critical Care Medical Center, Osaka Saiseikai Senri Hospital, Japan  
10  
11

12 3  
13

14 **Correspondence to**

15 Taku Iwami MD, PhD  
16  
17

18  
19  
20 6 Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501  
21  
22

23 7 Phone: +81-75-753-2426; Fax: +81-75-753-2424  
24  
25

26 8 E-mail: iwamit@e-mail.jp  
27  
28

29 9  
30  
31

32 10 **Total word count:** 2848 words (main text). **Abstract:** 276 words.  
33  
34

35 11  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 ABSTRACT**  
7

8  
9 **2 Objectives:** To evaluate epidemiological characteristics of out-of-hospital cardiac  
10  
11  
12 3 arrests (OHCAs) by detailed non-cardiac cause and factors associated with the  
13  
14  
15 4 outcomes after OHCAs with non-cardiac origin.  
16

17  
18 **5 Design:** A prospective, population-based observational study.  
19

20  
21 **6 Setting:** The Utstein Osaka Project.  
22

23  
24 **7 Participants:** 14,164 adult patients with OHCAs due to non-cardiac origin who were  
25  
26  
27 8 resuscitated by emergency-medical-service personnel or bystanders, and then were  
28  
29  
30 9 transported to medical institutions from January 2005 to December 2011.  
31

32  
33 **10 Primary outcome measures:** One-month survival after OHCA. Multiple logistic  
34  
35  
36 11 regression analysis was used to assess factors that were potentially associated with the  
37  
38  
39 12 outcome.  
40

41  
42 **13 Results:** During the study period, the one-month survival rate was 5.3% (755/14,164).  
43  
44  
45 14 The proportion of one-month survival was 6.2% (510/8239) in external causes, 6.5%  
46  
47  
48 15 (94/1148) in respiratory diseases, 0.8% (11/1309) in malignant tumors, 4.9% (55/1114)  
49  
50 16 in strokes, and 4.1% (85/2054) in others. As for external causes, the proportion of  
51  
52  
53 17 one-month survival was 14.3% (382/2670) in asphyxia, 4.2% (84/1999) in hanging,  
54  
55  
56 18 0.7% (9/1300) in fall, 1.1% (12/1062) in drowning, 1.6% (12/765) in traffic injury,  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 3.7% (7/187) in drug overuse, and 1.6% (4/256) in unclassified external causes. In a  
7  
8  
9 2 multivariate analysis, arrests witnessed by bystanders, good activities of daily living  
10  
11 3 before arrests, ventricular fibrillation arrests, public places, intravenous fluid, and early  
12  
13 4 emergency-medical-service response time were significant predictors for one-month  
14  
15 5 outcome after OHCA with cardiac origin. The proportion of one-month survival of the  
16  
17 6 whole OHCA with non-cardiac origin did not significantly increase (from 4.3%  
18  
19 7 [86/2023] in 2005 to 4.9% [105/2126] in 2011) and the adjusted odds ratio for  
20  
21 8 one-increment of year was 1.01 (95% confidence interval 0.97-1.06).  
22  
23  
24  
25  
26  
27  
28

29 9 **Conclusions:** From a large OHCA registry in Osaka, we demonstrated that one-month  
30  
31 10 survival after OHCA with non-cardiac origin was poor and stable.  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 Strengths and limitations of this study**  
7

8  
9 ■ This study showed that one-month survival after OHCA with non-cardiac origin  
10  
11 was poor and the survival trends did not improve year-by-year in Osaka during the  
12  
13 study period from 2005 to 2011. In addition, the survivals exceedingly differed by  
14  
15 detailed non-cardiac origin.  
16  
17  
18

19  
20 ■ The category of presumed non-cardiac causes is made clinically, as per the  
21  
22 Utstein-style international guidelines for cardiac arrest data reporting.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 INTRODUCTION

2 Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the  
3 industrialized world.<sup>1-4</sup> Although improvements in the chain of survival including the  
4 development of a public-access defibrillation system and revisions to cardiopulmonary  
5 resuscitation (CPR) guidelines have led to increased survival after OHCA with cardiac  
6 origin in some communities,<sup>5-7</sup> the outcome after OHCA with non-cardiac origin  
7 remains generally poor.<sup>7-13</sup>

8 Importantly, 20% to 40% of adult OHCA were reportedly of non-cardiac origin.<sup>7-13</sup>

9 However, epidemiological characteristics of OHCA with non-cardiac origin have not  
10 been sufficiently investigated as much as those of OHCA with cardiac origin.

11 Therefore, the evaluation of characteristics, trends, and outcomes by detailed  
12 non-cardiac cause and understanding the factors associated with the outcomes are  
13 needed to improve the survival after OHCA with non-cardiac origin.

14 The Utstein Osaka Project is a large prospective population-based cohort study of  
15 OHCA in Osaka, Japan, covering about 8.8 million residents.<sup>5</sup> During the 7 years from  
16 2005 to 2011, we enrolled approximately 14,000 OHCA with non-cardiac origin  
17 before emergency-medical-service (EMS) arrival. The present study aimed to evaluate  
18 the epidemiological characteristics of OHCA by detailed non-cardiac cause. In

1  
2  
3  
4  
5  
6 1 addition, we evaluated factors associated with the outcomes after OHCA with  
7  
8  
9 2 non-cardiac origin in a multivariate analysis.  
10  
11  
12 3

For peer review only

1  
2  
3  
4  
5  
6 **1 METHODS**

7  
8  
9 **2 Study design and setting**

10  
11  
12 The Utstein Osaka Project is a prospective, population-based registry of OHCA that is  
13  
14 based on the standardized Utstein style.<sup>14,15</sup> This study enrolled adult patients aged  
15  
16 =>20 years suffering OHCAs with non-cardiac origin before EMS arrival, who were  
17  
18 resuscitated by EMS personnel or bystanders, and were transported to medical  
19  
20 institutions in Osaka Prefecture from January 1, 2005 to December 31, 2011. In this  
21  
22 study, we excluded pediatric OHCA patients because characteristics and outcomes  
23  
24 from OHCAs differed between children and adults.<sup>16,17</sup>

25  
26  
27  
28  
29  
30  
31  
32 Cardiac arrest was defined as the cessation of cardiac mechanical activity as  
33  
34 confirmed by the absence of signs of circulation.<sup>14,15</sup> In this study, the arrests were  
35  
36 classified into those of presumed cardiac origin and non-cardiac origin, the latter  
37  
38 resulting from external causes, respiratory diseases, malignant tumors, strokes, and any  
39  
40 other non-cardiac causes based on hospital medical records. Furthermore, external  
41  
42 causes were divided into the seven categories: asphyxia, hanging, fall, drowning,  
43  
44 traffic injury, drug overuse, and unclassified external causes. These diagnoses were  
45  
46 made clinically by the physician in charge, working in collaboration with the EMS  
47  
48 personnel.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1

## 2 EMS organization in Osaka

3 Details of the EMS system in Osaka were described previously.<sup>5</sup> Osaka is the second  
4 largest prefecture in Japan with a population of approximately 8.8 million inhabitants  
5 in an area of 1892 km<sup>2</sup>. In Osaka, there are 34 fire stations with emergency dispatch  
6 centers. The EMS system is operated by the local fire stations. When called, an  
7 ambulance is dispatched from the nearest fire station. Emergency services are provided  
8 24 hours each day by them, which is single-tiered in 32 stations and two-tiered in two  
9 stations. The latter uses medics followed by physicians.

10 Most highly-trained prehospital emergency care providers are called Emergency  
11 Life-Saving Technicians (ELSTs). Usually, each ambulance has a crew of three  
12 emergency providers including at least one ELST. They were allowed to insert an  
13 intravenous line and an adjunct airway, and to use a semi-automated external  
14 defibrillator for OHCA patients. Specially trained ELSTs were permitted to tracheal  
15 intubation since July 2004 and administer intravenous epinephrine since April 2006.

16 Do-not-resuscitate (DNR) orders or living wills are not generally accepted in Japan.  
17 EMS providers are not permitted to terminate resuscitation in the field. Therefore,  
18 almost patients with OHCA who were treated by EMS personnel were transported to a



1 hospital and enrolled in the Utstein Osaka Project, excluding those with decapitation,  
2 incineration, decomposition, rigor mortis, or dependent cyanosis.

#### 4 **CPR and AED training for the general public**

5 The use of an automated external defibrillator (AED) by citizens was permitted legally  
6 in July 2004. In Osaka, approximately 14,000 citizens per year participated in the CPR  
7 training programs, consisting of conventional CPR including chest compressions,  
8 mouth-to-mouth ventilation, and AED usage by local fire departments, the Japan Red  
9 Cross, Inc., and the Osaka Life Support Association.<sup>5</sup> All EMS providers perform CPR  
10 according to the Japanese CPR guidelines.<sup>4</sup>

#### 12 **Data collection and quality control**

13 Data collection were prospectively conducted using a form that included data  
14 recommended in the Utstein-style reporting guidelines for cardiac arrests.<sup>14,15</sup> These  
15 data included gender, age, first documented cardiac rhythm, witness status, location of  
16 arrests, activity of daily living (ADL) before arrests, time-courses of resuscitation, type  
17 of bystander-initiated CPR, public-access AED use, intravascular fluid, tracheal  
18 intubation, and intravascular epinephrine as well as prehospital return of spontaneous

1  
2  
3  
4  
5  
6 1 circulation (ROSC), total ROSC, one-month survival, and neurological status one  
7  
8  
9 2 month after the event. First documented rhythm was recorded and diagnosed by the  
10  
11  
12 3 EMS personnel with semi-automated defibrillators on the scene, and confirmed by the  
13  
14  
15 4 physician who was responsible for the on-line medical direction. Bystander CPR  
16  
17  
18 5 included chest compression-only CPR and conventional CPR with rescue breathing. A  
19  
20  
21 6 series of EMS times of call receipt, vehicle arrival at the scene, contact with patients,  
22  
23  
24 7 initiation of CPR, defibrillation by EMS, and hospital arrival were recorded  
25  
26  
27 8 automatically at the dispatch center.

28  
29 9 The data form was completed by the EMS personnel in cooperation with the  
30  
31  
32 10 physicians in charge of the patients, and the data were integrated into the registry  
33  
34  
35 11 system on the Information Center for Emergency Medical Services of Osaka, and then  
36  
37  
38 12 checked by the investigators. If the data sheet was incomplete, the relevant EMS  
39  
40  
41 13 personnel were contacted and questioned for data completion.

42  
43  
44 14 All survivors suffering OHCA were followed up for up to one-month after the event  
45  
46  
47 15 by the EMS personnel in charge. One-month neurological outcomes were determined  
48  
49  
50 16 by the physician responsible for treating the patient, using the cerebral performance  
51  
52  
53 17 category (CPC) scale: category 1, good cerebral performance; category 2, moderate  
54  
55  
56 18 cerebral disability; category 3, severe cerebral disability; category 4, coma or  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 vegetative state; and category 5, death.<sup>14,15</sup>  
7  
8

9 2

10  
11 3 **Outcome measures**

12  
13  
14 4 The main outcome measure was one-month survival. Secondary outcome measures  
15  
16  
17 5 included prehospital and total ROSCs, admission to hospital, and one-month survival  
18  
19  
20 6 with neurologically favorable outcome. Neurologically favorable outcome was defined  
21  
22  
23 7 as CPC category 1 or 2.<sup>14,15</sup>  
24  
25

26 8

27  
28  
29 9 **Statistical analysis**

30  
31  
32 10 In this study, patient and EMS characteristics of OHCAs with non-cardiac origin and  
33  
34  
35 11 their outcomes were compared between the groups using unpaired analysis of variance  
36  
37  
38 12 for numerical variables, and chi-square test or Fisher's exact test for categorical  
39  
40  
41 13 variables by cause of arrest. First, non-cardiac causes were divided into the following  
42  
43  
44 14 five groups; external causes, respiratory diseases, malignant tumors, strokes, and any  
45  
46  
47 15 other non-cardiac causes. Next, external causes were further divided into asphyxia,  
48  
49  
50 16 hanging, fall, drowning, traffic injury, drug overuse, and unclassified external causes.  
51  
52  
53 17 Age-adjusted annual incidence of OHCAs by non-cardiac origin was calculated by the  
54  
55  
56 18 direct method using 2005 census data and 1985 Japanese model population.<sup>18,19</sup>  
57  
58  
59  
60

1 Poisson regression models for the trends in the incidence and one-month survival rate  
2 were used. Multiple logistic regression analysis assessed the factors associated with  
3 one-month survival and neurological favorable outcome, and adjusted odds ratios  
4 (AORs) and their 95% confidence intervals (CIs) were calculated. As potential  
5 confounders, factors that were biologically essential and considered to be associated  
6 with clinical outcomes were taken in the multivariable analyses.<sup>7</sup> These variables  
7 included age (20-64, >=65 years old), gender (men, women), witness status (none,  
8 witnessed by bystanders), ADL before arrests (good, other), first documented rhythm  
9 (VF, non-VF), bystander CPR status (none, compression-only CPR, conventional CPR),  
10 type of non-cardiac causes (the 11 categories described above), location of arrests  
11 (homes, public places, work places, health care facilities, others), intravascular fluid  
12 (yes, no), intubation (yes, no), epinephrine (yes, no), EMS response time (call to  
13 contact with patients), and year of arrest. In addition, we conducted a multivariate  
14 analysis of one-month survival from OHCA with non-cardiac origin after dividing the  
15 two groups: internal (respiratory diseases, malignant tumors, and strokes) and external  
16 (asphyxia, hanging, fall, drowning, traffic injury, and drug overuse) causes.

17 All statistical analyses were performed using the SPSS statistical package ver21.0J  
18 (IBM Corp. Armonk, NY). All of the tests were 2-tailed and *P* values of <0.05 were

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 considered statistically significant.

2

For peer review only

## 1 RESULTS

2 Figure 1 shows an overview of the study patients based on the Utstein template. A total  
3 of 47,735 adult arrests were documented during these seven years. Resuscitation was  
4 attempted in 43,845, and 15,505 of them were of non-cardiac origin. Excluding 1341  
5 victims who were witnessed by EMS (arrests after EMS arrival), 14,164 (5561 in  
6 bystander-witnessed cases and 8603 in non-witnessed cases) were eligible for our  
7 analyses. Among these arrests, 8239 (58.2%) were due to external causes, 1448  
8 (10.2%) respiratory diseases, 1309 (9.2%) malignant tumors, 1114 (7.9%) strokes, and  
9 2054 (14.5%) others. Among external causes, 2670 (16.5%) were of asphyxia, 1999  
10 (14.1%) hanging, 1300 (9.2%) fall, 1062 (7.5%) drowning, 765 (5.4%) traffic injury,  
11 and 256 (1.8%) unclassified external cause.

12 The age-adjusted annual incidence rates per 100,000 persons by non-cardiac cause  
13 were calculated over time (Table 1). The incidence rate of OHCA with external  
14 causes significantly increased from 12.4 in 2005 to 13.3 in 2011 (P for trend=0.024).  
15 The incidence rate significantly decreased among OHCA patients with respiratory  
16 diseases (from 2.2 in 2005 to 1.6 in 2011, P for trend=0.018) and strokes (from 2.0 in  
17 2005 to 1.3 in 2011, P for trend<0.001). The unadjusted one-month survival rates by  
18 non-cardiac cause were almost stable during the study period.

1 Patient and EMS characteristics of OHCA with non-cardiac origin according to the  
2 cause are shown in Table 2, and their outcomes in Table 4. The mean age of all OHCA  
3 patients with non-cardiac origin was 66.8 years and males were 58.0%. The proportion  
4 of bystander-witnessed arrests, ADL before arrests, first documented rhythm, type of  
5 bystander CPR, and advanced life supports such as intravascular fluid, intubation, and  
6 epinephrine exceedingly varied between the five groups. In the whole patients, the rate  
7 of one-month survival and neurologically favorable outcome was 5.3% and 1.3%. The  
8 proportion of one-month survival was 6.2% in external causes, 6.5% in respiratory  
9 diseases, 0.8% in malignant tumors, 4.9% in strokes, and 4.1% in others. Furthermore,  
10 patient and EMS characteristics of OHCA in external causes are shown in Table 3,  
11 and their outcomes in Table 5. The characteristics and outcomes varied between the  
12 seven groups. The proportion of one-month survival was 14.3% in asphyxia, 4.2% in  
13 hanging, 0.7% in fall, 1.1% in submersion, 1.6% in traffic injury, 3.7% in drug overuse,  
14 and 1.6% in unclassified external cause. The proportion of bystander chest  
15 compression-only CPR and conventional CPR with rescue breathing was 23.2% and  
16 13.1% in whole OHCA with non-cardiac origin, and 22.1% and 14.3% in  
17 bystander-witnessed OHCA.

18 Table 6 shows factors contributing to one-month survival and neurologically

1 favorable outcome after OHCAs with non-cardiac origin. In one-month survival,  
2 arrests witnessed by bystanders (AOR 4.13, 95% CI 3.35-5.09), good ADL before  
3 arrests (AOR 1.23, 95% CI 1.03-1.47), VF as first documented rhythm (AOR 2.04,  
4 95% CI 1.42-2.92), public places (AOR 1.45, 95% CI 1.10-1.91), intravenous fluid  
5 (AOR 1.45, 95% CI 1.14-1.84), and early EMS response time (AOR for one-increment  
6 of minute 0.92, 95% CI 0.90-.095) were associated with improving outcome. However,  
7 type of bystander CPR, intubation, and epinephrine were not associated with better  
8 outcome. Compared with asphyxia, the AORs were significantly lower in respiratory  
9 diseases (0.51, 95% CI 0.40-0.65), malignant tumors (0.06, 95% CI 0.03-0.11), stroke  
10 (0.27, 95% CI 0.20-0.38), hanging (0.56, 95% CI 0.41-0.77), fall (0.03, 95% CI  
11 0.01-0.06), drowning (0.16, 95% CI 0.09-0.29), and traffic injury (0.05, 95% CI  
12 0.03-0.10). The proportion of one-month survival of the whole OHCAs with  
13 non-cardiac origin did not significantly increase (from 4.3% [86/2023] in 2005 to 4.9%  
14 [105/2126] in 2011) and the AOR for one-increment of year was 1.01 (95% CI  
15 0.97-1.06). The AORs of neurologically favorable outcome after OHCAs with  
16 non-cardiac origin were almost similar to those of one-month survival.

17 Subgroup analyses after dividing the two groups (internal and external causes) are  
18 shown in Supplemental Table. As for internal causes, arrests witnessed by bystanders



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 (AOR 2.86, 95% CI 1.99-4.11), VF as first documented rhythm (AOR 2.35, 95% CI  
2 1.30-4.24), and public places (AOR 2.01, 95% CI 1.21-3.36) were associated with  
3 improving outcome. As for external causes, adults (AOR 1.51, 95% CI 1.17-1.96),  
4 arrests witnessed by bystanders (AOR 5.03, 95% CI 3.71-6.81), good ADL before  
5 arrests (AOR 1.34, 95% CI 1.08-1.67), intravenous fluid (AOR 1.69, 95% CI  
6 1.27-2.25), and early EMS response time (AOR for one-increment of minute 0.93, 95%  
7 CI 0.90-0.96) were associated with improving outcome.

For peer review only

1  
2  
3  
4  
5  
6 **1 DISCUSSION**  
7

8  
9 2 The extensive OHCA registry in Osaka showed that one-month survival after OHCAs  
10  
11 3 with non-cardiac origin was poor and the survival trends did not improve year-by-year.

12  
13  
14 4 In addition, the survivals differed by detailed non-cardiac origin. To further improve  
15  
16 5 survival after OHCAs, sufficient attention should be paid to the epidemiological  
17  
18 6 characteristics of OHCAs with non-cardiac origin as much as those of OHCA with  
19  
20 7 cardiac origin, and this study describing the actual situation regarding the incidence  
21  
22 8 and outcome of OHCAs with non-cardiac origin provides valuable information to  
23  
24 9 improve the survival.  
25  
26  
27  
28  
29  
30  
31

32 10 Our study observed that the outcomes of OHCAs with non-cardiac origin were poor  
33  
34 11 and stable during the seven years. In a previous study in Japan, neurologically  
35  
36 12 favorable outcome of bystander-witnessed OHCAs with non-cardiac origin increased  
37  
38 13 from 2005 to 2011, but the absolute survival was very low,<sup>7</sup> and this result was similar  
39  
40 14 with ours. Improving the outcome of OHCAs with non-cardiac origin poses an  
41  
42 15 important problem in resuscitation science because 20~40% of adult OHCAs are of  
43  
44 16 non-cardiac origin.<sup>7-13</sup> In addition, the survivals exceedingly differed by detailed  
45  
46 17 non-cardiac origin, which also suggests the need and importance of an origin-specific  
47  
48 18 strategy for improving the outcomes.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 We also showed that the OHCA incidence trends differed by detailed non-cardiac  
2 origin. For instance, the incidence rate of OHCA due to strokes significantly  
3 decreased during the study period. Although the reasons for the decrement were  
4 unclear, better blood pressure control and decreasing smoking rate in recent years of  
5 Japan might be one of the possible explanations for this phenomenon.<sup>20</sup> In fact, the  
6 numbers of stroke patients in Japan has also been decreasing.<sup>21</sup> On the other hand, the  
7 incidence rates of OHCA with external causes increased and the outcomes after  
8 OHCA with external causes excluding asphyxia were miserable. For example,  
9 external OHCA due to trauma, drug overdose, or hanging in metropolitan area of  
10 Australia were more common and the survivals from traumatic and hanging-associated  
11 OHCA were not always futile. Therefore, there were regional variations on the  
12 incidence and outcome from OHCA with external causes,<sup>22,23</sup> and the  
13 countermeasures would differ by regions. However, most importantly, more efforts  
14 should focus on prevention of OHCA with external causes because many of them are  
15 preventable.<sup>1-4</sup>

16 In a multivariable analysis, intravenous fluid administration was associated with  
17 better one-month survival after OHCA with non-cardiac origin. In preceding studies,  
18 prehospital intravenous fluid for OHCA including both cardiac and non-cardiac

1 origins was not associated with the improved outcome,<sup>24</sup> whereas intravenous access  
2 were associated with a reduction in hospital mortality among non-injured, non-cardiac  
3 arrest patients<sup>25</sup> Thus, the effects of fluid administration on prehospital emergency  
4 patients were under debate, and further investigations by other cohorts or randomized  
5 controlled trials are needed to confirm these associations.

6 In this study, a multivariate analysis also underscored that either bystander-initiated  
7 chest compression-only CPR or conventional CPR with rescue breathing was not  
8 effective for OHCA with non-cardiac origin. From a nationwide study focused on  
9 43,000 bystander-witnessed OHCA with non-cardiac origin, we demonstrated that  
10 conventional CPR with rescue breathing had an incremental benefit for OHCA with  
11 non-cardiac origin, but the impact on the overall survival after OHCA was small.<sup>8</sup>  
12 Considering these results, the effectiveness of bystander CPR on OHCA with  
13 non-cardiac origin might be limited. In addition, attempted resuscitation rates in our  
14 area was exceedingly higher at 92% compared with those in western countries,<sup>22,26</sup>  
15 which might be also one of the possible explanations for the lack of impact of  
16 bystander CPR in our multivariate model. However, as recommended in the CPR  
17 guidelines,<sup>1-4</sup> bystander CPR plays a key role in the “chain of survival” and increasing  
18 the proportion of bystander CPR for OHCA patients is important.

1  
2  
3  
4  
5  
6 1 Furthermore, factors such as arrests witnessed by bystanders and earlier EMS  
7  
8  
9 2 response time were also independent predictors of better outcome after OHCA with  
10  
11  
12 3 non-cardiac origin in a multivariate analysis. This would indicate the importance of an  
13  
14 4 early EMS activation in the chain of survival<sup>1-4</sup> and suggests that activating the EMS  
15  
16  
17 5 system quickly leads to improving the outcomes after OHCA with non-cardiac origin.  
18  
19  
20 6 In addition, the verification of the effects on prehospital emergency care as well as  
21  
22  
23 7 in-hospital treatment is essential to improve survival after OHCA with non-cardiac  
24  
25  
26 8 origin.

27  
28  
29 9 The present study has some inherent limitations. First, the category of presumed  
30  
31  
32 10 cardiac or non-cardiac causes is made clinically, as per the Utstein-style international  
33  
34  
35 11 guidelines for cardiac arrest data reporting.<sup>14,15</sup> Second, information on post-arrest care  
36  
37  
38 12 is lacking. In-hospital treatment (e.g., hemodynamic support, cardiovascular  
39  
40  
41 13 intervention, induced hypothermia) might affect survival after OHCA.<sup>27</sup> Third,  
42  
43  
44 14 unmeasured confounding factors may have influenced the association between OHCA  
45  
46  
47 15 with non-cardiac origin and the outcome.

48  
49  
50 16

## 51 52 17 **CONCLUSION**

53  
54  
55 18 The large OHCA registry in Osaka demonstrated that one-month survival after OHCA  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 with non-cardiac origin was poor, the survival trends did not improve year-by-year, and  
7  
8  
9 2 the survivals differed by detailed non-cardiac origin. Further monitoring and discussion  
10  
11  
12 3 for epidemiology and outcome of OHCA with non-cardiac origin are warranted to  
13  
14  
15 4 improve survival after OHCA in this group.  
16  
17  
18 5  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 Acknowledgments**  
7

8  
9 2 We are deeply indebted to all of the EMS personnel and concerned physicians in Osaka  
10  
11 3 Prefecture, and the Osaka Medical Association for their indispensable cooperation and  
12  
13 4 generous support. We also thank all members of the Utstein Osaka Project for their  
14  
15 5 contribution in the organization, coordination, and oversight as the steering committee.  
16  
17  
18  
19  
20  
21  
22

23 **7 Contributors**  
24

25  
26 8 All authors (TK, KK, TS, TI, CN, KK, TN, YH, YK, KY, and TS) participated in the study  
27  
28 9 conception and design, acquisition of data, analysis and interpretation of data, drafting the  
29  
30 10 article and revising it critically for important intellectual content, and final approval of the  
31  
32 11 manuscript.  
33  
34  
35  
36  
37  
38  
39  
40

41 **13 Funding**  
42

43  
44 14 This study was supported by a scientific research grant from the Ministry of Health, Labour,  
45  
46 15 and Welfare of Japan (25112601).  
47  
48  
49  
50

51  
52 **17 Competing interests**  
53

54  
55 18 None.  
56  
57  
58  
59  
60

1

2 **Ethics approval**

3 The study was approved by the institutional review board of Osaka University with the assent  
4 of the EMS authorities of the local governments in Osaka Prefecture.

5

6 **Provenance and peer review**

7 Not commissioned; externally peer reviewed.

8

9 **Data sharing statement**

10 TK had full access to all of the data in the study and takes responsibility for the integrity of the  
11 data and the accuracy of the data analysis.

12

13 **Open Access**

14 This is an Open Access article distributed in accordance with the Creative Commons  
15 Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute,  
16 remix, adapt, build upon this work noncommercially, and license their derivative works on  
17 different terms, provided the original work is properly cited and the use is non-commercial.

18 See: <http://creativecommons.org/licenses/by-nc/3.0/>

19



1  
2  
3  
4  
5  
6 **1 REFERENCES**  
7

- 8  
9 2 1. 2010 International consensus on cardiopulmonary resuscitation and emergency  
10  
11  
12 3 cardiovascular care science with treatment recommendations. *Circulation*  
13  
14 4 2010;122:S250-605.  
15  
16  
17 5 2. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and  
18  
19  
20 6 emergency cardiovascular care. *Circulation* 2010;122:S639-946.  
21  
22  
23 7 3. European Resuscitation Council Guidelines for Resuscitation 2010. *Resuscitation*  
24  
25  
26 8 2010;81:1219-451.  
27  
28  
29 9 4. 2010 Japanese guidelines for emergency care and cardiopulmonary resuscitation. 1st ed.  
30  
31  
32 10 Tokyo: Health Shuppansha; 2011 (in Japanese).  
33  
34  
35 11 5. Iwami T, Nichol G, Hiraide A, *et al.* Continuous improvements of chain of survival  
36  
37  
38 12 increased survival after out-of-hospital cardiac arrests: a large-scale population-based  
39  
40  
41 13 study. *Circulation* 2009;119:728-34.  
42  
43  
44 14 6. Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation  
45  
46  
47 15 during out-of-hospital ventricular fibrillation arrest: survival implications of guideline  
48  
49  
50 16 changes. *Circulation* 2006;114:2760-5.  
51  
52  
53 17 7. Kitamura T, Iwami T, Kawamura T, *et al.* Nationwide improvements in survival from  
54  
55  
56 18 out-of-hospital cardiac arrests in Japan. *Circulation* 2012;126:2834-43.  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 8. Kitamura T, Iwami T, Kawamura T, *et al.* Bystander-initiated rescue breathing for  
7  
8  
9 2 out-of-hospital cardiac arrests of non-cardiac origin. *Circulation* 2010;122:293-9.  
10  
11  
12 3 9. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin.  
13  
14 4 Epidemiology and outcome. *Eur Heart J* 1997;18:1122-8.  
15  
16  
17 5 10. Engdahl J, Bång A, Karlson BW, *et al.* Characteristics and outcome among patients  
18  
19 6 suffering from out of hospital cardiac arrest of non-cardiac aetiology. *Resuscitation*  
20  
21 7 2003;57:33-41.  
22  
23  
24  
25  
26 8 11. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital  
27  
28 9 cardiac arrest of non-cardiac origin. *Resuscitation* 2007;72:200-7.  
29  
30  
31  
32 10 12. Iwami T, Hiraide A, Nakanishi N, *et al.* Age and sex analyses of out-of-hospital cardiac  
33  
34 11 arrest in Osaka, Japan. *Resuscitation* 2003;57:145-52.  
35  
36  
37  
38 12 13. Engdahl J, Holmberg M, Karlson BW, *et al.* The epidemiology of out-of-hospital ‘sudden’  
39  
40 13 cardiac arrest. *Resuscitation* 2002;52:235-45.  
41  
42  
43  
44 14 14. Cummins RO, Chamberlain DA, Abramson NS, *et al.* Recommended guideline for  
45  
46 15 uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style: a statement  
47  
48 16 for health professionals from a task force of the American Heart Association, the  
49  
50 17 European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the  
51  
52 18 Australian Resuscitation Council. *Circulation* 1991;84:960-75.  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 15. Jacobs I, Nadkarni V, Bahr J, *et al.* Cardiac arrest and cardiopulmonary resuscitation  
7  
8  
9 2 outcome reports: update and simplification of the Utstein templates for resuscitation  
10  
11 3 registries: a statement for healthcare professionals from a task force of the International  
12  
13 4 Liaison Committee on Resuscitation (American Heart Association, European  
14  
15 Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation  
16  
17 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
18  
19 Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.  
20  
21  
22  
23  
24  
25  
26 8 16. Nitta M, Iwami T, Kitamura T, *et al.* Age-specific differences in outcomes after  
27  
28  
29 9 out-of-hospital cardiac arrests. *Pediatrics* 2011;128:e812-20.  
30  
31  
32 10 17. Atkins DL, Everson-Stewart S, Sears GK, *et al.* Epidemiology and outcomes from  
33  
34  
35 11 out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium  
36  
37  
38 12 Epistry-Cardiac Arrest. *Circulation* 2009;119:1484-91.  
39  
40  
41 13 18. 2010 Population Census of Japan.  
42  
43  
44 14 [http://www.stat.go.jp/data/kokusei/2010/index.htm?utm\\_source=twitterfeed&utm\\_mediu](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter)  
45  
46  
47 15 [m=twitter](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter) (Accessed August 05, 2014) (in Japanese).  
48  
49  
50 16 19. Vital Statistics of Japan 2005. Tokyo: Health and Welfare Statistics Association; 2007.  
51  
52  
53 17 20. Hata J, Ninomiya T, Hirakawa Y, *et al.* Secular trends in cardiovascular disease and its  
54  
55  
56 18 risk factors in Japanese: half-century data from the Hisayama Study (1961-2009).  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 *Circulation* 2013;128:1198-205.  
7  
8  
9 2 21. 2011 Overview of Patient Survey. <http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/>  
10  
11  
12 3 (Accessed August 05, 2014) (in Japanese).  
13  
14 4 22. Deasy C, Bray J, Smith K, *et al.* Traumatic out-of-hospital cardiac arrests in Melbourne,  
15  
16  
17 5 Australia. *Resuscitation* 2012;83:465-70.  
18  
19  
20 6 23. Deasy C, Bray J, Smith K, *et al.* Hanging-associated out-of-hospital cardiac arrests in  
21  
22  
23 7 Melbourne, Australia. *Emerg Med J* 2013;30:38-42.  
24  
25  
26 8 24. Hagihara A, Hasegawa M, Abe T, *et al.* Prehospital lactated ringer's solution treatment  
27  
28  
29 9 and survival in out-of-hospital cardiac arrest: a prospective cohort analysis. *PLoS Med*  
30  
31  
32 10 2013;10:e1001394.  
33  
34  
35 11 25. Seymour CW, Cooke CR, Hebert PL, *et al.* Intravenous access during out-of-hospital  
36  
37  
38 12 emergency care of noninjured patients: a population-based outcome study. *Ann Emerg*  
39  
40  
41 13 *Med* 2012;59:296-303.  
42  
43  
44 14 26. Nichol G, Thomas E, Callaway CW, *et al.* Regional variation in out-of-hospital cardiac  
45  
46  
47 15 arrest incidence and outcome. *JAMA* 2008;300:1423-31.  
48  
49  
50 16 27. Neumar RW, Nolan JP, Adrie C, *et al.* Post-cardiac arrest syndrome: epidemiology,  
51  
52  
53 17 pathophysiology, treatment, and prognostication. A Scientific Statement from the  
54  
55  
56 18 International Liaison Committee on Resuscitation; the American Heart Association  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1       Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and  
2  
3       Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the  
4  
5       Council on Clinical Cardiology; the Council on Stroke. *Circulation* 2008;118:2452-8.

For peer review only

1  
2  
3  
4  
5  
6 **1 Figure Legends**  
7

8  
9 **2 Figure 1** Overview of EMS-treated cardiac arrests with an abridged Utstein template from  
10  
11  
12 3 January 1, 2005 to December 31, 2011. EMS, emergency medical service.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

Table 1 Age-adjusted incidences and unadjusted one-month survival rate of out-of-hospital cardiac arrests with non-cardiac origin according to the cause over time

	2005	2006	2007	2008	2009	2010	2011	P for trend
Age-adjusted Incidence per 100,000 persons								
External causes	12.4	12.3	13.2	12.8	13.2	13.3	13.3	0.024
Asphyxia	2.7	3.0	2.8	3.4	3.1	2.9	2.9	0.726
Hanging	3.4	3.4	4.1	3.4	3.7	3.9	3.9	0.158
Fall	2.4	2.5	3.1	2.4	2.9	3.0	2.7	0.396
Drowning	1.2	1.1	1.2	1.4	1.2	1.3	1.6	0.065
Traffic injury	1.6	1.5	1.4	1.4	1.4	1.5	1.4	0.229
Drug overdose	0.5	0.4	0.2	0.4	0.4	0.4	0.3	0.304
Unclassified	0.5	0.5	0.4	0.3	0.5	0.4	0.5	0.447
Respiratory diseases	2.2	1.8	1.8	1.7	1.3	1.3	1.6	0.018
Malignant tumors	1.6	1.8	1.8	1.7	1.5	1.3	1.6	0.109
Strokes	2.0	1.8	1.8	1.6	1.4	1.2	1.3	< 0.001
Others	2.7	3.3	3.1	2.9	2.7	2.5	2.4	0.087
Unadjusted one-month survival, % (n/N)								
External causes	4.8 (53/1100)	6.8 (72/1059)	5.7 (66/1164)	7.2 (85/1184)	7.1 (86/1207)	6.1 (75/1225)	5.6 (73/1300)	0.736
Asphyxia	10.4 (35/337)	15.4 (53/344)	13.0 (44/338)	15.6 (67/430)	16.3 (66/406)	14.8 (58/393)	14.0 (59/422)	0.374
Hanging	4.6 (12/261)	4.7 (12/255)	5 (16/318)	4.8 (13/273)	4.9 (14/287)	3.3 (10/301)	2.3 (7/304)	0.101
Fall	0.6 (1/159)	0.6 (1/169)	0.9 (2/219)	1.2 (2/165)	0.0 (0/197)	0.5 (1/208)	1.1 (2/183)	NA
Drowning	1.3 (2/151)	3.3 (4/120)	0.0 (0/128)	1.3 (2/159)	2.1 (3/144)	0.7 (1/148)	0.0 (0/212)	NA
Traffic injury	0.9 (1/116)	1.0 (1/101)	1.8 (2/109)	0.9 (1/106)	1.9 (2/103)	1.7 (2/115)	2.6 (3/115)	0.027

Drug overdose	3.0 (1/33)	0.0 (0/29)	5.6 (1/18)	0.0 (0/25)	3.3 (1/30)	11.1 (3/27)	4.0 (1/25)	NA
Unclassified	2.3 (1/43)	2.4 (1/41)	2.9 (1/34)	0.0 (0/26)	0.0 (0/40)	0.0 (0/33)	2.6 (1/39)	NA
Respiratory diseases	6.4 (17/267)	3.9 (8/206)	8.0 (17/212)	9.8 (21/214)	6.7 (11/165)	4.7 (8/169)	5.6 (12/215)	0.875
Malignant tumors	0.5 (1/186)	0.5 (1/194)	1.0 (2/202)	1.0 (2/196)	0.0 (0/178)	2.5 (4/159)	0.5 (1/194)	NA
Strokes	3.6 (7/196)	6.1 (11/179)	4.5 (8/176)	3.2 (5/154)	4.9 (7/143)	6.0 (8/134)	6.8 (9/132)	0.241
Others	2.9 (8/277)	7.0 (22/314)	1.3 (4/308)	4.5 (14/311)	4.3 (12/278)	5.3 (15/281)	3.5 (10/285)	0.808

NA indicates not analyzed.

Peer review only



**Table 2** Patient and EMS characteristics of out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n=14,164)	External causes (n = 8239)	Respiratory diseases (n=1448)	Malignant tumors (n=1309)	Strokes (n=1114)	Others (n=2054)	<i>P</i> value*
Age, yr, mean (SD)	66.8 (19.0)	63.5 (20.5)	76.1 (14.2)	71.9 (12.0)	67.7 (14.7)	69.8 (17.6)	< 0.001
Age group, n (%)							< 0.001
Adults aged 20-64 years	5513 (38.9)	3826 (46.4)	229 (15.8)	345 (26.4)	447 (40.1)	666 (32.4)	
Elderly aged >=65 years	8651 (61.1)	4413 (53.6)	1219 (84.2)	964 (73.6)	667 (59.9)	1388 (67.6)	
Men, n (%)	8215 (58.0)	4789 (58.1)	844 (58.3)	881 (67.3)	559 (50.2)	1142 (55.6)	< 0.001
Arrests witnessed by bystanders, n (%)	5561 (39.3)	2952 (35.8)	682 (47.1)	639 (48.8)	493 (44.3)	795 (38.7)	< 0.001
Good activities of daily living, n (%)	8522 (60.2)	5213 (63.3)	653 (45.1)	443 (33.8)	896 (80.4)	1317 (64.1)	< 0.001
First documented rhythm, n (%)							< 0.001
VF	324 (2.3)	119 (1.4)	35 (2.4)	26 (2.0)	69 (6.2)	75 (3.7)	
PEA	3356 (23.7)	1853 (22.5)	394 (27.2)	262 (20.0)	329 (29.5)	518 (25.2)	
Asystole	10196 (72.0)	6124 (74.3)	983 (67.9)	1008 (77.0)	647 (58.1)	1434 (69.8)	
Others	288 (2.0)	143 (1.7)	36 (2.5)	13 (1.0)	69 (6.2)	27 (1.3)	
Location of arrest, n (%)							< 0.001
Homes	9010 (63.6)	4435 (53.8)	1098 (75.8)	1217 (93.0)	801 (71.9)	1459 (71.0)	
Public places	2035 (14.4)	1608 (19.5)	59 (4.1)	24 (1.8)	156 (14.0)	188 (9.2)	
Work places	346 (2.4)	223 (2.7)	7 (0.5)	4 (0.3)	48 (4.3)	64 (3.1)	
Health care facilities	1505 (10.6)	904 (11.0)	248 (17.1)	55 (4.2)	63 (5.7)	235 (11.4)	
Others	1268 (9.0)	1069 (13.0)	36 (2.5)	9 (0.7)	46 (4.1)	108 (5.3)	
Public-access AED use, n (%)	13 (0.1)	4 (0.05)	2 (0.1)	0 (0.0)	5 (0.4)	2 (0.1)	0.001
Type of Bystander CPR, n (%)							< 0.001
No CPR	9023 (63.7)	5383 (65.3)	836 (57.7)	889 (67.9)	633 (56.8)	1282 (62.4)	
Chest compression-only CPR	3288 (23.2)	1811 (22.0)	408 (28.2)	297 (22.7)	283 (25.4)	489 (23.8)	

Conventional CPR with rescue breathing	1853 (13.1)	1045 (12.7)	204 (14.1)	123 (9.4)	198 (17.8)	283 (13.8)	
Intravascular fluid, n (%)	2320 (16.4)	1458 (17.7)	202 (14.0)	113 (8.6)	230 (20.6)	317 (15.4)	< 0.001
Intubation, n (%)	2639 (18.6)	1364 (16.6)	338 (23.3)	242 (18.5)	257 (23.1)	438 (21.3)	< 0.001
Epinephrine, n (%)	987 (7.0)	572 (6.9)	88 (6.1)	49 (3.7)	125 (11.2)	153 (7.4)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.9 (4.1)	8.0 (4.6)	7.7 (3.0)	7.7 (2.7)	7.7 (2.8)	7.9 (3.8)	0.003
Call to CPR by EMS, min, mean (SD)	8.5 (4.5)	8.8 (5.1)	8.1 (3.1)	8.1 (2.8)	8.2 (2.9)	8.4 (4.2)	< 0.001
Call to hospital arrival, min, mean (SD)	28.2 (8.6)	28.4 (8.6)	27.3 (8.2)	28.0 (8.9)	28.2 (8.4)	28.1 (8.7)	0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 3** Patient and EMS characteristics of out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Age, yr, mean (SD)	77.9 (14.4)	55.6 (17.4)	47.4 (17.4)	73.1 (14.8)	52.6 (19.0)	49.9 (19.5)	58.1 (19.3)	< 0.001
Age group, n (%)								< 0.001
Adults aged 20-64 years	403 (15.1)	1136 (66.8)	1055 (81.2)	210 (19.8)	523 (68.4)	141 (75.4)	158 (61.7)	
Elderly aged ≥65 years	2267 (84.9)	663 (33.2)	245 (18.8)	852 (80.2)	242 (31.6)	46 (24.6)	98 (38.3)	
Men, n (%)	1345 (50.4)	1290 (64.5)	781 (60.1)	530 (49.9)	558 (72.9)	117 (62.6)	168 (65.6)	< 0.001
Arrests witnessed by bystanders, n (%)	1801 (67.5)	27 (1.4)	510 (39.2)	56 (5.3)	476 (62.2)	10 (5.3)	72 (28.1)	< 0.001
Good activities of daily living, n (%)	1099 (41.2)	1769 (88.5)	685 (52.7)	854 (80.4)	517 (67.6)	133 (71.1)	156 (60.9)	< 0.001
First documented rhythm, n (%)								< 0.001
VF	56 (2.1)	13 (0.7)	19 (1.5)	12 (1.1)	14 (1.8)	1 (0.5)	4 (1.6)	
PEA	960 (36.0)	198 (9.9)	274 (21.1)	72 (6.8)	259 (33.9)	20 (10.7)	70 (27.3)	
Asystole	1589 (59.5)	1775 (88.8)	985 (75.8)	970 (91.3)	469 (61.3)	160 (85.6)	176 (68.8)	
Others	65 (2.4)	13 (0.7)	22 (1.7)	8 (0.8)	23 (3.0)	6 (3.2)	6 (2.3)	
Location of arrest, n (%)								< 0.001
Homes	1596 (59.8)	1667 (83.4)	139 (10.7)	770 (72.5)	2 (0.3)	150 (80.2)	111 (43.4)	
Public places	139 (5.2)	86 (4.3)	553 (42.5)	83 (7.8)	677 (88.5)	14 (7.5)	56 (21.9)	
Workplaces	35 (1.3)	94 (4.7)	44 (3.4)	3 (0.3)	7 (0.9)	7 (3.7)	33 (12.9)	
Health care facilities	835 (31.3)	27 (1.4)	12 (0.9)	14 (1.3)	1 (0.1)	0 (0.0)	15 (5.9)	
Others	65 (2.4)	125 (6.3)	552 (42.5)	192 (18.1)	78 (10.2)	16 (8.6)	41 (16.0)	

Public-access AED use, n (%)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.214
Type of Bystander CPR, n (%)									< 0.001
No CPR	1386 (51.9)	1174 (58.7)	1191 (91.6)	608 (57.3)	673 (88.0)	154 (82.4)	197 (77.0)		
Chest compression-only CPR	748 (28.0)	549 (27.5)	93 (7.2)	281 (26.5)	74 (9.7)	23 (12.3)	43 (16.8)		
Conventional CPR with rescue breathing	536 (20.1)	276 (13.8)	16 (1.2)	173 (16.3)	18 (2.4)	10 (5.3)	16 (6.2)		
Intravascular fluid, n (%)	540 (20.2)	393 (19.7)	107 (8.2)	281 (26.5)	76 (9.9)	27 (14.4)	34 (13.3)	< 0.001	
Intubation, n (%)	800 (30.0)	167 (8.4)	41 (3.2)	251 (23.6)	31 (4.1)	33 (17.6)	41 (16.0)	< 0.001	
Epinephrine, n (%)	326 (12.2)	83 (4.2)	41 (3.2)	68 (6.4)	37 (4.8)	6 (3.2)	11 (4.3)	< 0.001	
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.6 (2.9)	7.8 (3.3)	7.4 (3.3)	9.4 (7.6)	7.6 (4.2)	14.2 (10.7)	9.4 (7.3)	< 0.001	
Call to CPR by EMS personnel, min, mean (SD)	7.9 (3.1)	8.6 (3.9)	8.2 (3.8)	10.0 (7.5)	9.3 (5.9)	14.4 (10.0)	11.0 (8.7)	< 0.001	
Call to hospital arrival, min, mean (SD)	28.6 (8.6)	28.2 (7.9)	27.5 (8.3)	29.1 (9.3)	27.1 (8.8)	32.1 (11.1)	29.5 (9.4)	< 0.001	

\*P values are calculated to test the homogeneity among the 7 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 4** Outcomes after out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 1,4164)	External causes (n = 8239)	Respiratory diseases (n = 1448)	Malignant tumors (n = 1309)	Strokes (n = 1114)	Others (n =2054)	<i>P</i> value *
Prehospital ROSC, n (%)	1229 (8.7)	703 (8.5)	114 (7.9)	57 (4.4)	216 (19.4)	139 (6.8)	< 0.001
Total ROSC, n (%)	4744 (33.5)	2638 (32.0)	620 (42.8)	234 (17.9)	650 (58.3)	602 (29.3)	< 0.001
Hospital admission, n (%)	4142 (29.2)	2356 (28.6)	530 (36.6)	173 (13.2)	585 (52.5)	498 (24.2)	< 0.001
One-month survival, n (%)	755 (5.3)	510 (6.2)	94 (6.5)	11 (0.8)	55 (4.9)	85 (4.1)	< 0.001
Neurologically favorable outcome, n (%)	188 (1.3)	105 (1.3)	27 (1.9)	2 (0.2)	17 (1.5)	37 (1.8)	< 0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

ROSC indicates return of spontaneous circulation.

**Table 5** Outcomes after out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value *
Prehospital ROSC, n (%)	463 (17.3)	144 (7.2)	22 (1.7)	36 (3.4)	28 (3.7)	4 (2.1)	6 (2.3)	< 0.001
Total ROSC, n (%)	1003 (37.6)	1500 (75.0)	1213 (93.3)	894 (84.2)	637 (83.3)	143 (76.5)	211 (82.4)	< 0.001
Hospital admission, n (%)	1529 (57.3)	453 (22.7)	62 (4.8)	147 (13.8)	92 (12.0)	40 (21.4)	33 (12.9)	< 0.001
One-month survival, n (%)	382 (14.3)	84 (4.2)	9 (0.7)	12 (1.1)	12 (1.6)	7 (3.7)	4 (1.6)	< 0.001
Neurologically favorable outcome, n (%)	71 (2.7)	17 (0.9)	1 (0.1)	4 (0.4)	6 (0.8)	4 (2.1)	2 (0.8)	< 0.001

\**P* values are calculated to test the homogeneity among the 7 cause groups.

ROSC indicates return of spontaneous circulation.

**Table 6** Factors associated with outcomes after out-of-Hospital cardiac arrests with non-cardiac origin

	One-month survival				Neurologically favorable outcome			
	Crude OR	(95% CI)	Adjusted OR	(95% CI)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	0.95	(0.82-1.10)	1.36	(1.12-1.65)	1.02	(0.76-1.37)	1.52	(1.07-2.15)
Men	0.75	(0.64-0.88)	0.99	(0.84-1.16)	1.09	(0.81-1.46)	0.91	(0.67-1.24)
Witnessed by bystanders	4.41	(3.74-5.19)	4.13	(3.35-5.09)	4.48	(3.23-6.21)	4.83	(3.21-7.29)
Good activities of daily living	0.93	(0.80-1.08)	1.23	(1.03-1.47)	1.39	(1.02-1.88)	1.43	(1.02-2.02)
VF	2.74	(1.96-3.82)	2.04	(1.42-2.92)	7.72	(5.05-11.79)	5.40	(3.40-8.59)
Type of bystander CPR								
No CPR	Reference		Reference		Reference		Reference	
Chest compression-only CPR	0.97	(0.81-1.16)	0.80	(0.66-0.98)	0.95	(0.67-1.35)	0.92	(0.64-1.33)
Conventional CPR with rescue breathing	1.47	(1.20-1.79)	1.07	(0.86-1.34)	1.01	(0.65-1.55)	0.89	(0.56-1.42)
Type of non-cardiac origin								
Respiratory diseases	0.42	(0.33-0.53)	0.51	(0.40-0.65)	0.70	(0.44-1.09)	0.76	(0.48-1.21)
Malignant tumors	0.05	(0.03-0.09)	0.06	(0.03-0.11)	0.06	(0.01-0.23)	0.06	(0.01-0.23)
Strokes	0.31	(0.23-0.42)	0.27	(0.20-0.38)	0.57	(0.33-0.97)	0.34	(0.19-0.61)
Asphyxia	Reference		Reference		Reference		Reference	
Hanging	0.26	(0.21-0.34)	0.56	(0.41-0.77)	0.31	(0.18-0.53)	0.55	(0.28-1.07)
Fall	0.04	(0.02-0.08)	0.03	(0.01-0.06)	0.03	(0.004-0.20)	0.01	(0.002-0.11)
Drowning	0.07	(0.04-0.12)	0.16	(0.09-0.29)	0.14	(0.05-0.38)	0.31	(0.11-0.90)

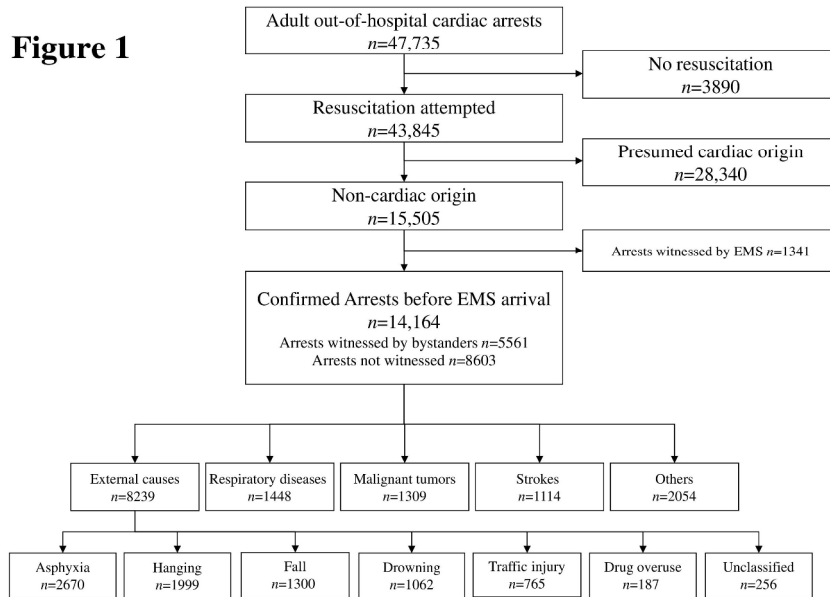
Traffic injury	0.10 (0.05-0.17)	0.05 (0.03-0.10)	0.29 (0.13-0.67)	0.10 (0.04-0.26)
Drug overdose	0.23 (0.11-0.50)	0.58 (0.26-1.29)	0.80 (0.29-2.21)	1.74 (0.58-5.19)
Others	0.26 (0.20-0.33)	0.29 (0.22-0.38)	0.67 (0.45-1.00)	0.60 (0.39-0.92)
Unclassified	0.10 (0.04-0.26)	0.10 (0.04-0.28)	0.29 (0.07-1.18)	0.27 (0.06-1.16)
Location of arrest				
Homes	Reference	Reference	Reference	Reference
Public places	0.78 (0.61-0.99)	1.45 (1.10-1.91)	1.11 (0.75-1.65)	1.54 (0.97-2.44)
Workplaces	1.29 (0.83-1.98)	1.40 (0.87-2.23)	1.26 (0.55-2.89)	0.95 (0.39-2.30)
Health care facilities	1.69 (1.38-2.07)	0.88 (0.69-1.12)	0.72 (0.42-1.24)	0.47 (0.26-0.85)
Others	0.70 (0.51-0.94)	1.67 (1.19-2.35)	0.68 (0.38-1.24)	1.35 (0.72-2.54)
Intravascular fluid	1.78 (1.50-2.11)	1.45 (1.14-1.84)	1.34 (0.94-1.91)	1.52 (0.97-2.38)
Intubation	1.62 (1.37-1.92)	1.02 (0.84-1.23)	0.73 (0.48-1.10)	0.50 (0.32-0.77)
Epinephrine	2.32 (1.87-2.88)	0.97 (0.71-1.32)	1.25 (0.74-2.09)	0.60 (0.31-1.17)
EMS response time (for one-increment of minute)	0.93 (0.91-0.96)	0.92 (0.90-0.95)	0.91 (0.86-0.96)	0.90 (0.84-0.95)
Year (for one-increment of year)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.02 (0.95-1.09)	1.05 (0.97-1.13)

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Figure 1



297x209mm (300 x 300 DPI)

view only

**Supplemental Table** Factors associated with one-month survival after out-of-hospital cardiac arrests with non-cardiac origin by internal and external causes

	One-month survival			
	Internal causes		External causes	
	Adjusted OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	1.01	(0.68 - 1.50)	1.51	(1.17 - 1.96)
Men	0.99	(0.71 - 1.40)	0.91	(0.75 - 1.11)
Witnessed by bystanders	2.86	(1.99 - 4.11)	5.03	(3.71 - 6.81)
Good activities of daily living	1.27	(0.87 - 1.85)	1.34	(1.08 - 1.67)
VF	2.35	(1.30 - 4.24)	0.44	(0.17 - 1.11)
Type of bystander CPR				
No CPR	Reference		Reference	
Chest compression-only CPR	0.66	(0.43 - 1.01)	0.79	(0.61 - 1.01)
Conventional CPR with rescue breathing	0.83	(0.51 - 1.36)	1.18	(0.89 - 1.54)
Type of non-cardiac origin				
Respiratory diseases	Reference		--	
Malignant tumors	0.12	(0.06 - 0.23)	--	
Strokes	0.55	(0.37 - 0.82)	--	
Asphyxia	--		Reference	
Hanging	--		0.60	(0.41 - 0.87)
Fall	--		0.03	(0.01 - 0.06)
Drowning	--		0.05	(0.03 - 0.11)
Traffic injury	--		0.17	(0.09 - 0.31)
Drug overdose	--		0.60	(0.26 - 1.36)
Location of arrest				
Homes	Reference		Reference	
Public places	2.01	(1.21 - 3.36)	1.39	(0.94 - 2.04)
Workplaces	1.88	(0.69 - 5.15)	1.47	(0.77 - 2.80)
Health care facilities	1.00	(0.55 - 1.81)	0.82	(0.62 - 1.09)
Others	2.10	(0.99 - 4.47)	1.72	(1.12 - 2.63)
Intravascular fluid	0.65	(0.33 - 1.29)	1.69	(1.27 - 2.25)
Intubation	0.62	(0.39 - 0.97)	1.21	(0.96 - 1.52)
Epinephrine	1.89	(0.82 - 4.34)	0.93	(0.64 - 1.35)
EMS response time (for one-increment of minute)	0.97	(0.91 - 1.03)	0.93	(0.90 - 0.96)
Year (for one-increment of year)	1.02	(0.94 - 1.11)	1.01	(0.96 - 1.06)

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

# BMJ Open

## Epidemiology and outcome of adult out-of-hospital cardiac arrest with non-cardiac origin in Osaka: a population-based study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-006462.R2
Article Type:	Research
Date Submitted by the Author:	03-Nov-2014
Complete List of Authors:	Kitamura, Tetsuhisa; Osaka University, Graduate School of Medicine Kiyohara, Kosuke; Tokyo Women's Medical University, Sakai, Tomohiko; Osaka University, Department of Traumatology and Acute Critical Medicine Iwami, Taku ; Kyoto University , Health Service Nishiyama, Chika; Kyoto University, Department of Critical Care Nursing Kajino, Kentaro; Osaka National Hospital, Traumatology and Critical Care Medical Center Nishiuchi, Tatsuya; Kinki University, Department of Acute Medicine Hayashi, Yasuyuki; Osaka Saiseikai Senri Hospital, Senri Critical Care Medical Center Katayama, Yusuke; Osaka University, Department of Traumatology and Acute Critical Medicine Yoshiya, Kazuhisa; Osaka University, Department of Traumatology and Acute Critical Medicine Shimazu, Takeshi; Osaka University, Department of Traumatology and Acute Critical Medicine
<b>Primary Subject Heading</b>:	Emergency medicine
Secondary Subject Heading:	Epidemiology, Cardiovascular medicine
Keywords:	ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY, Adult intensive & critical care < INTENSIVE & CRITICAL CARE

SCHOLARONE™  
Manuscripts

1 **Epidemiology and outcome of adult out-of-hospital cardiac arrest**  
2 **with non-cardiac origin in Osaka: a population-based study**

3  
4 Tetsuhisa Kitamura,<sup>1</sup> Kosuke Kiyohara,<sup>2</sup> Tomohiko Sakai,<sup>3</sup> Taku Iwami,<sup>4</sup> Chika Nishiyama,<sup>5</sup>  
5 Kentaro Kajino,<sup>6</sup> Tatsuya Nishiuchi,<sup>7</sup> Yasuyuki Hayashi,<sup>8</sup> Yusuke Katayama,<sup>3</sup> Kazuhisa  
6 Yoshiya,<sup>3</sup> Takeshi Shimazu<sup>3</sup>

7  
8 **Author affiliations**

9 <sup>1</sup>Division of Environmental Medicine and Population Sciences, Department of Social and  
10 Environmental Medicine, Graduate School of Medicine, Osaka University, Japan

11 <sup>2</sup>Department of Public Health, Tokyo Women's Medical University, Japan

12 <sup>3</sup>Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School  
13 of Medicine, Japan

14 <sup>4</sup>Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto, Japan

15 <sup>5</sup>Department of Critical Care Nursing, Graduate School of Medicine and School of Health  
16 Sciences, Kyoto University, Japan

17 <sup>6</sup>Traumatology and Critical Care Medical Center, National Hospital Organization Osaka  
18 National Hospital, Japan

1  
2  
3  
4  
5  
6 1 <sup>7</sup>Department of Acute Medicine, Kinki University Faculty of Medicine, Japan  
7

8  
9 2 <sup>8</sup>Senri Critical Care Medical Center, Osaka Saiseikai Senri Hospital, Japan  
10

11  
12 3

13  
14 4 **Correspondence to**

15 Taku Iwami MD, PhD

16  
17  
18  
19  
20 6 Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501  
21

22  
23 7 Phone: +81-75-753-2426; Fax: +81-75-753-2424  
24

25  
26 8 E-mail: iwamit@e-mail.jp  
27

28  
29 9  
30

31  
32 10 **Total word count:** 2857 words (main text). **Abstract:** 285 words.  
33

34  
35 11  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 **1 ABSTRACT**  
7

8  
9 **2 Objectives:** To evaluate epidemiological characteristics of out-of-hospital cardiac  
10  
11  
12 **3 arrests (OHCAs)** by detailed non-cardiac cause and factors associated with the  
13  
14  
15 **4 outcomes** after OHCAs with non-cardiac origin.  
16

17  
18 **5 Design:** A prospective, population-based observational study.  
19

20  
21 **6 Setting:** The Utstein Osaka Project.  
22

23  
24 **7 Participants:** 14,164 adult patients aged  $\geq 20$  years old with OHCAs due to  
25  
26  
27 **8 non-cardiac origin** who were resuscitated by emergency-medical-service personnel or  
28  
29  
30 **9 bystanders**, and then were transported to medical institutions from January 2005 to  
31  
32 **10 December 2011**.  
33

34  
35 **11 Primary outcome measures:** One-month survival after OHCA. Multiple logistic  
36  
37  
38 **12 regression analysis** was used to assess factors that were potentially associated with the  
39  
40  
41 **13 outcome**.  
42

43  
44 **14 Results:** During the study period, the one-month survival rate was 5.3% (755/14,164).  
45

46  
47 **15 The proportion** of one-month survival was 6.2% (510/8239) in external causes, 6.5%  
48  
49  
50 **16 (94/1148)** in respiratory diseases, 0.8% (11/1309) in malignant tumors, 4.9% (55/1114)  
51  
52  
53 **17 in strokes**, and 4.1% (85/2054) in others. As for external causes, the proportion of  
54  
55  
56 **18 one-month survival** was 14.3% (382/2670) in asphyxia, 4.2% (84/1999) in hanging,  
57  
58  
59  
60



1 0.7% (9/1300) in fall, 1.1% (12/1062) in drowning, 1.6% (12/765) in traffic injury,  
2 3.7% (7/187) in drug overuse, and 1.6% (4/256) in unclassified external causes. In a  
3 multivariate analysis, adults aged <65 years old, arrests witnessed by bystanders, good  
4 activities of daily living before arrests, ventricular fibrillation arrests, public places,  
5 intravenous fluid, and early emergency-medical-service response time were significant  
6 predictors for one-month outcome after OHCA with non-cardiac origin. The  
7 proportion of one-month survival of the whole OHCA with non-cardiac origin did not  
8 significantly increase (from 4.3% [86/2023] in 2005 to 4.9% [105/2126] in 2011) and  
9 the adjusted odds ratio for one-increment of year was 1.01 (95% confidence interval  
10 0.97-1.06).

11 **Conclusions:** From a large OHCA registry in Osaka, we demonstrated that one-month  
12 survival after OHCA with non-cardiac origin was poor and stable.

13

1  
2  
3  
4  
5  
6 **1 Strengths and limitations of this study**  
7

8  
9 ■ This study showed that one-month survival after OHCA with non-cardiac origin  
10  
11 was poor and the survival trends did not improve year-by-year in Osaka during the  
12  
13 study period from 2005 to 2011. In addition, the survivals exceedingly differed by  
14  
15 detailed non-cardiac origin.  
16  
17  
18

19  
20 ■ The category of presumed non-cardiac causes is made clinically, as per the  
21  
22 Utstein-style international guidelines for cardiac arrest data reporting.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 INTRODUCTION

2 Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the  
3 industrialized world.<sup>1-4</sup> Although improvements in the chain of survival including the  
4 development of a public-access defibrillation system and revisions to cardiopulmonary  
5 resuscitation (CPR) guidelines have led to increased survival after OHCA with cardiac  
6 origin in some communities,<sup>5-7</sup> the outcome after OHCA with non-cardiac origin  
7 remains generally poor.<sup>7-13</sup>

8 Importantly, 20% to 40% of adult OHCA were reportedly of non-cardiac origin.<sup>7-13</sup>  
9 However, epidemiological characteristics of OHCA with non-cardiac origin have not  
10 been sufficiently investigated as much as those of OHCA with cardiac origin.  
11 Therefore, the evaluation of characteristics, trends, and outcomes by detailed  
12 non-cardiac cause and understanding the factors associated with the outcomes are  
13 needed to improve the survival after OHCA with non-cardiac origin.

14 The Utstein Osaka Project is a large prospective population-based cohort study of  
15 OHCA in Osaka, Japan, covering about 8.8 million residents.<sup>5</sup> During the 7 years from  
16 2005 to 2011, we enrolled approximately 14,000 OHCA with non-cardiac origin  
17 before emergency-medical-service (EMS) arrival. The present study aimed to evaluate  
18 the epidemiological characteristics of OHCA by detailed non-cardiac cause. In

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 addition, we evaluated factors associated with the outcomes after OHCA with  
2 non-cardiac origin in a multivariate analysis.  
3

For peer review only

1  
2  
3  
4  
5  
6 **1 METHODS**

7  
8  
9 **2 Study design and setting**

10  
11  
12 3 The Utstein Osaka Project is a prospective, population-based registry of OHCA that is  
13  
14 4 based on the standardized Utstein style.<sup>14,15</sup> This study enrolled adult patients aged  
15  
16  
17 5 =>20 years suffering OHCAs with non-cardiac origin before EMS arrival, who were  
18  
19  
20 6 resuscitated by EMS personnel or bystanders, and were transported to medical  
21  
22  
23 7 institutions in Osaka Prefecture from January 1, 2005 to December 31, 2011. In this  
24  
25  
26 8 study, we excluded pediatric OHCA patients because characteristics and outcomes  
27  
28  
29 9 from OHCAs differed between children and adults.<sup>16,17</sup>

30  
31  
32 10 Cardiac arrest was defined as the cessation of cardiac mechanical activity as  
33  
34  
35 11 confirmed by the absence of signs of circulation.<sup>14,15</sup> In this study, the arrests were  
36  
37  
38 12 classified into those of presumed cardiac origin and non-cardiac origin, the latter  
39  
40  
41 13 resulting from external causes, respiratory diseases, malignant tumors, strokes, and any  
42  
43  
44 14 other non-cardiac causes based on hospital medical records. Furthermore, external  
45  
46  
47 15 causes were divided into the seven categories: asphyxia, hanging, fall, drowning,  
48  
49  
50 16 traffic injury, drug overuse, and unclassified external causes. These diagnoses were  
51  
52  
53 17 made clinically by the physician in charge, working in collaboration with the EMS  
54  
55  
56 18 personnel.

1

## 2 EMS organization in Osaka

3 Details of the EMS system in Osaka were described previously.<sup>5</sup> Osaka is the second  
4 largest prefecture in Japan with a population of approximately 8.8 million inhabitants  
5 in an area of 1892 km<sup>2</sup>. In Osaka, there are 34 fire stations with emergency dispatch  
6 centers. The EMS system is operated by the local fire stations. When called, an  
7 ambulance is dispatched from the nearest fire station. Emergency services are provided  
8 24 hours each day by them, which is single-tiered in 32 stations and two-tiered in two  
9 stations. The latter uses medics followed by physicians.

10 Most highly-trained prehospital emergency care providers are called Emergency  
11 Life-Saving Technicians (ELSTs). Usually, each ambulance has a crew of three  
12 emergency providers including at least one ELST. They were allowed to insert an  
13 intravenous line and an adjunct airway, and to use a semi-automated external  
14 defibrillator for OHCA patients. Specially trained ELSTs were permitted to tracheal  
15 intubation since July 2004 and administer intravenous epinephrine since April 2006.

16 Do-not-resuscitate (DNR) orders or living wills are not generally accepted in Japan.  
17 EMS providers are not permitted to terminate resuscitation in the field. Therefore,  
18 almost patients with OHCA who were treated by EMS personnel were transported to a

1 hospital and enrolled in the Utstein Osaka Project, excluding those with decapitation,  
2 incineration, decomposition, rigor mortis, or dependent cyanosis.

#### 3 4 **CPR and AED training for the general public**

5 The use of an automated external defibrillator (AED) by citizens was permitted legally  
6 in July 2004. In Osaka, approximately 14,000 citizens per year participated in the CPR  
7 training programs, consisting of conventional CPR including chest compressions,  
8 mouth-to-mouth ventilation, and AED usage by local fire departments, the Japan Red  
9 Cross, Inc., and the Osaka Life Support Association.<sup>5</sup> All EMS providers perform CPR  
10 according to the Japanese CPR guidelines.<sup>4</sup>

#### 11 12 **Data collection and quality control**

13 Data collection were prospectively conducted using a form that included data  
14 recommended in the Utstein-style reporting guidelines for cardiac arrests.<sup>14,15</sup> These  
15 data included gender, age, first documented cardiac rhythm, witness status, location of  
16 arrests, activity of daily living (ADL) before arrests, time-courses of resuscitation, type  
17 of bystander-initiated CPR, public-access AED use, intravascular fluid, tracheal  
18 intubation, and intravascular epinephrine as well as prehospital return of spontaneous

1  
2  
3  
4  
5  
6 1 circulation (ROSC), total ROSC, one-month survival, and neurological status one  
7  
8  
9 2 month after the event. First documented rhythm was recorded and diagnosed by the  
10  
11  
12 3 EMS personnel with semi-automated defibrillators on the scene, and confirmed by the  
13  
14  
15 4 physician who was responsible for the on-line medical direction. Bystander CPR  
16  
17  
18 5 included chest compression-only CPR and conventional CPR with rescue breathing. A  
19  
20  
21 6 series of EMS times of call receipt, vehicle arrival at the scene, contact with patients,  
22  
23  
24 7 initiation of CPR, defibrillation by EMS, and hospital arrival were recorded  
25  
26  
27 8 automatically at the dispatch center.

28  
29 9 The data form was completed by the EMS personnel in cooperation with the  
30  
31  
32 10 physicians in charge of the patients, and the data were integrated into the registry  
33  
34  
35 11 system on the Information Center for Emergency Medical Services of Osaka, and then  
36  
37  
38 12 checked by the investigators. If the data sheet was incomplete, the relevant EMS  
39  
40  
41 13 personnel were contacted and questioned for data completion.

42  
43  
44 14 All survivors suffering OHCA were followed up for up to one-month after the event  
45  
46  
47 15 by the EMS personnel in charge. One-month neurological outcomes were determined  
48  
49  
50 16 by the physician responsible for treating the patient, using the cerebral performance  
51  
52  
53 17 category (CPC) scale: category 1, good cerebral performance; category 2, moderate  
54  
55  
56 18 cerebral disability; category 3, severe cerebral disability; category 4, coma or  
57  
58  
59  
60



1 vegetative state; and category 5, death.<sup>14,15</sup>

2

### 3 **Outcome measures**

4 The main outcome measure was one-month survival. Secondary outcome measures  
5 included prehospital and total ROSCs, admission to hospital, and one-month survival  
6 with neurologically favorable outcome. Neurologically favorable outcome was defined  
7 as CPC category 1 or 2.<sup>14,15</sup>

### 9 **Statistical analysis**

10 In this study, patient and EMS characteristics of OHCAs with non-cardiac origin and  
11 their outcomes were compared between the groups using unpaired analysis of variance  
12 for numerical variables, and chi-square test or Fisher's exact test for categorical  
13 variables by cause of arrest. First, non-cardiac causes were divided into the following  
14 five groups; external causes, respiratory diseases, malignant tumors, strokes, and any  
15 other non-cardiac causes. Next, external causes were further divided into asphyxia,  
16 hanging, fall, drowning, traffic injury, drug overuse, and unclassified external causes.  
17 Age-adjusted annual incidence of OHCAs by non-cardiac origin was calculated by the  
18 direct method using 2005 census data and 1985 Japanese model population.<sup>18,19</sup>

1  
2  
3  
4  
5  
6 1 Poisson regression models for the trends in the incidence and one-month survival rate  
7  
8  
9 2 were used. Multiple logistic regression analysis assessed the factors associated with  
10  
11  
12 3 one-month survival and neurological favorable outcome, and adjusted odds ratios  
13  
14 4 (AORs) and their 95% confidence intervals (CIs) were calculated. As potential  
15  
16  
17 5 confounders, factors that were biologically essential and considered to be associated  
18  
19  
20 6 with clinical outcomes were taken in the multivariable analyses.<sup>7</sup> These variables  
21  
22  
23 7 included age (20-64, ≥65 years old), gender (men, women), witness status (none,  
24  
25  
26 8 witnessed by bystanders), ADL before arrests (good, other), first documented rhythm  
27  
28  
29 9 (VF, non-VF), bystander CPR status (none, compression-only CPR, conventional CPR),  
30  
31  
32 10 type of non-cardiac causes (the 11 categories described above), location of arrests  
33  
34  
35 11 (homes, public places, work places, health care facilities, others), intravascular fluid  
36  
37  
38 12 (yes, no), intubation (yes, no), epinephrine (yes, no), EMS response time (call to  
39  
40  
41 13 contact with patients), and year of arrest. In addition, we conducted a multivariate  
42  
43  
44 14 analysis of one-month survival from OHCA with non-cardiac origin after dividing the  
45  
46  
47 15 two groups: internal (respiratory diseases, malignant tumors, and strokes) and external  
48  
49  
50 16 (asphyxia, hanging, fall, drowning, traffic injury, and drug overuse) causes.

51  
52 17 All statistical analyses were performed using the SPSS statistical package ver21.0J  
53  
54  
55 18 (IBM Corp. Armonk, NY). All of the tests were 2-tailed and *P* values of <0.05 were  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 considered statistically significant.  
7  
8

9 2  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## 1 RESULTS

2 Figure 1 shows an overview of the study patients based on the Utstein template. A total  
3 of 47,735 adult arrests were documented during these seven years. Resuscitation was  
4 attempted in 43,845, and 15,505 of them were of non-cardiac origin. Excluding 1341  
5 victims who were witnessed by EMS (arrests after EMS arrival), 14,164 (5561 in  
6 bystander-witnessed cases and 8603 in non-witnessed cases) were eligible for our  
7 analyses. Among these arrests, 8239 (58.2%) were due to external causes, 1448  
8 (10.2%) respiratory diseases, 1309 (9.2%) malignant tumors, 1114 (7.9%) strokes, and  
9 2054 (14.5%) others. Among external causes, 2670 (16.5%) were of asphyxia, 1999  
10 (14.1%) hanging, 1300 (9.2%) fall, 1062 (7.5%) drowning, 765 (5.4%) traffic injury,  
11 and 256 (1.8%) unclassified external cause. We could not obtain information on  
12 one-month survival and neurological status for 7 (0.05%) among 14,164 eligible  
13 victims.

14 The age-adjusted annual incidence rates per 100,000 persons by non-cardiac cause  
15 were calculated over time (Table 1). The incidence rate of OHCA with external  
16 causes significantly increased from 12.4 in 2005 to 13.3 in 2011 (P for trend=0.024).  
17 The incidence rate significantly decreased among OHCA patients with respiratory  
18 diseases (from 2.2 in 2005 to 1.6 in 2011, P for trend=0.018) and strokes (from 2.0 in

1  
2  
3  
4  
5  
6 1 2005 to 1.3 in 2011, P for trend<0.001). The unadjusted one-month survival rates by  
7  
8  
9 2 non-cardiac cause were almost stable during the study period.

10  
11 Patient and EMS characteristics of OHCAs with non-cardiac origin according to the  
12  
13 cause are shown in Table 2, and their outcomes in Table 4. The mean age of all OHCA  
14  
15 patients with non-cardiac origin was 66.8 years and males were 58.0%. The proportion  
16  
17 of bystander-witnessed arrests, ADL before arrests, first documented rhythm, type of  
18  
19 bystander CPR, and advanced life supports such as intravascular fluid, intubation, and  
20  
21 epinephrine exceedingly varied between the five groups. In the whole patients, the rate  
22  
23 of one-month survival and neurologically favorable outcome was 5.3% and 1.3%. The  
24  
25 proportion of one-month survival was 6.2% in external causes, 6.5% in respiratory  
26  
27 diseases, 0.8% in malignant tumors, 4.9% in strokes, and 4.1% in others. Furthermore,  
28  
29 patient and EMS characteristics of OHCAs in external causes are shown in Table 3,  
30  
31 and their outcomes in Table 5. The characteristics and outcomes varied between the  
32  
33 seven groups. The proportion of one-month survival was 14.3% in asphyxia, 4.2% in  
34  
35 hanging, 0.7% in fall, 1.1% in submersion, 1.6% in traffic injury, 3.7% in drug overuse,  
36  
37 and 1.6% in unclassified external cause. The proportion of bystander chest  
38  
39 compression-only CPR and conventional CPR with rescue breathing was 23.2% and  
40  
41 13.1% in whole OHCAs with non-cardiac origin, and 22.1% and 14.3% in  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 bystander-witnessed OHCAs.

2 Table 6 shows factors contributing to one-month survival and neurologically  
3 favorable outcome after OHCAs with non-cardiac origin. In one-month survival, adults  
4 aged <65 years old (AOR 1.36, 95% CI 1.12-1.65), arrests witnessed by bystanders  
5 (AOR 4.13, 95% CI 3.35-5.09), good ADL before arrests (AOR 1.23, 95% CI  
6 1.03-1.47), VF as first documented rhythm (AOR 2.04, 95% CI 1.42-2.92), public  
7 places (AOR 1.45, 95% CI 1.10-1.91), intravenous fluid (AOR 1.45, 95% CI  
8 1.14-1.84), and early EMS response time (AOR for one-increment of minute 0.92, 95%  
9 CI 0.90-0.95) were associated with improving outcome. However, type of bystander  
10 CPR, intubation, and epinephrine were not associated with better outcome. Compared  
11 with asphyxia, the AORs were significantly lower in respiratory diseases (0.51, 95%  
12 CI 0.40-0.65), malignant tumors (0.06, 95% CI 0.03-0.11), stroke (0.27, 95% CI  
13 0.20-0.38), hanging (0.56, 95% CI 0.41-0.77), fall (0.03, 95% CI 0.01-0.06), drowning  
14 (0.16, 95% CI 0.09-0.29), and traffic injury (0.05, 95% CI 0.03-0.10). The proportion  
15 of one-month survival of the whole OHCAs with non-cardiac origin did not  
16 significantly increase (from 4.3% [86/2023] in 2005 to 4.9% [105/2126] in 2011) and  
17 the AOR for one-increment of year was 1.01 (95% CI 0.97-1.06). The AORs of  
18 neurologically favorable outcome after OHCAs with non-cardiac origin were almost

1 similar to those of one-month survival.

2 Subgroup analyses after dividing the two groups (internal and external causes) are  
3 shown in Supplemental Table. As for internal causes, arrests witnessed by bystanders  
4 (AOR 2.86, 95% CI 1.99-4.11), VF as first documented rhythm (AOR 2.35, 95% CI  
5 1.30-4.24), and public places (AOR 2.01, 95% CI 1.21-3.36) were associated with  
6 improving outcome. As for external causes, adults (AOR 1.51, 95% CI 1.17-1.96),  
7 arrests witnessed by bystanders (AOR 5.03, 95% CI 3.71-6.81), good ADL before  
8 arrests (AOR 1.34, 95% CI 1.08-1.67), intravenous fluid (AOR 1.69, 95% CI  
9 1.27-2.25), and early EMS response time (AOR for one-increment of minute 0.93, 95%  
10 CI 0.90-0.96) were associated with improving outcome.

11

1  
2  
3  
4  
5  
6 **1 DISCUSSION**  
7

8  
9 2 The extensive OHCA registry in Osaka showed that one-month survival after OHCA  
10  
11 3 with non-cardiac origin was poor and the survival trends did not improve year-by-year.

12  
13  
14 4 In addition, the survivals differed by detailed non-cardiac origin. To further improve  
15  
16 5 survival after OHCA, sufficient attention should be paid to the epidemiological  
17  
18 6 characteristics of OHCA with non-cardiac origin as much as those of OHCA with  
19  
20 7 cardiac origin, and this study describing the actual situation regarding the incidence  
21  
22 8 and outcome of OHCA with non-cardiac origin provides valuable information to  
23  
24 9 improve the survival.  
25  
26  
27  
28  
29  
30  
31

32 10 Our study observed that the outcomes of OHCA with non-cardiac origin were poor  
33  
34 11 and stable during the seven years. In a previous study in Japan, neurologically  
35  
36 12 favorable outcome of bystander-witnessed OHCA with non-cardiac origin increased  
37  
38 13 from 2005 to 2011, but the absolute survival was very low,<sup>7</sup> and this result was similar  
39  
40 14 with ours. Improving the outcome of OHCA with non-cardiac origin poses an  
41  
42 15 important problem in resuscitation science because 20~40% of adult OHCA are of  
43  
44 16 non-cardiac origin.<sup>7-13</sup> In addition, the survivals exceedingly differed by detailed  
45  
46 17 non-cardiac origin, which also suggests the need and importance of an origin-specific  
47  
48 18 strategy for improving the outcomes.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1 We also showed that the OHCA incidence trends differed by detailed non-cardiac  
2 origin. For instance, the incidence rate of OHCA due to strokes significantly  
3 decreased during the study period. Although the reasons for the decrement were  
4 unclear, better blood pressure control and decreasing smoking rate in recent years of  
5 Japan might be one of the possible explanations for this phenomenon.<sup>20</sup> In fact, the  
6 numbers of stroke patients in Japan has also been decreasing.<sup>21</sup> On the other hand, the  
7 incidence rates of OHCA with external causes in our region increased and the  
8 outcomes after OHCA with external causes excluding asphyxia were miserable.  
9 However, there were regional variations on the incidence and outcome from OHCA  
10 with external causes.<sup>22,23</sup> For example, external OHCA due to trauma, drug overdose,  
11 or hanging in metropolitan area of Australia were more common and the survivals from  
12 traumatic and hanging-associated OHCA were not always futile, and the  
13 countermeasures would, therefore, differ by regions. Most importantly, more efforts  
14 should focus on prevention of OHCA with external causes because many of them are  
15 preventable.<sup>1-4</sup>

16 In a multivariable analysis, intravenous fluid administration was associated with  
17 better one-month survival after OHCA with non-cardiac origin. In preceding studies,  
18 prehospital intravenous fluid for OHCA including both cardiac and non-cardiac

1 origins was not associated with the improved outcome,<sup>24</sup> whereas intravenous access  
2 were associated with a reduction in hospital mortality among non-injured, non-cardiac  
3 arrest patients<sup>25</sup> Thus, the effects of fluid administration on prehospital emergency  
4 patients were under debate, and further investigations by other cohorts or randomized  
5 controlled trials are needed to confirm these associations.

6 In this study, a multivariate analysis also underscored that either bystander-initiated  
7 chest compression-only CPR or conventional CPR with rescue breathing was not  
8 effective for OHCA with non-cardiac origin. From a nationwide study focused on  
9 43,000 bystander-witnessed OHCA with non-cardiac origin, we demonstrated that  
10 conventional CPR with rescue breathing had an incremental benefit for OHCA with  
11 non-cardiac origin, but the impact on the overall survival after OHCA was small.<sup>8</sup>  
12 Considering these results, the effectiveness of bystander CPR on OHCA with  
13 non-cardiac origin in our region might be related to the significantly high rates of  
14 attempted EMS resuscitation in Japan compared with western countries.<sup>22,26</sup> However,  
15 as recommended in the CPR guidelines,<sup>1-4</sup> bystander CPR plays a key role in the  
16 “chain of survival” and increasing the proportion of bystander CPR for OHCA patients  
17 is important.

18 Furthermore, factors such as arrests witnessed by bystanders and earlier EMS

1  
2  
3  
4  
5  
6 1 response time were also independent predictors of better outcome after OHCA with  
7  
8  
9 2 non-cardiac origin in a multivariate analysis. This would indicate the importance of an  
10  
11 3 early EMS activation in the chain of survival<sup>1-4</sup> and suggests that activating the EMS  
12  
13 4 system quickly leads to improving the outcomes after OHCA with non-cardiac origin.  
14  
15  
16  
17 5 In addition, the verification of the effects on prehospital emergency care as well as  
18  
19  
20 6 in-hospital treatment is essential to improve survival after OHCA with non-cardiac  
21  
22  
23 7 origin.  
24

25  
26 8 The present study has some inherent limitations. First, the category of presumed  
27  
28 9 cardiac or non-cardiac causes is made clinically, as per the Utstein-style international  
29  
30 10 guidelines for cardiac arrest data reporting.<sup>14,15</sup> Second, information on post-arrest care  
31  
32 11 is lacking. In-hospital treatment (e.g., hemodynamic support, cardiovascular  
33  
34 12 intervention, induced hypothermia) might affect survival after OHCA.<sup>27</sup> Third,  
35  
36 13 unmeasured confounding factors may have influenced the association between OHCA  
37  
38 14 with non-cardiac origin and the outcome.  
39  
40  
41  
42  
43  
44  
45

46  
47 15

## 48 49 16 **CONCLUSION**

50  
51  
52 17 The large OHCA registry in Osaka demonstrated that one-month survival after OHCA  
53  
54 18 with non-cardiac origin was poor, the survival trends did not improve year-by-year, and  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 the survivals differed by detailed non-cardiac origin. Further monitoring and discussion  
2 for epidemiology and outcome of OHCA with non-cardiac origin are warranted to  
3 improve survival after OHCA in this group.

4

For peer review only

1  
2  
3  
4  
5  
6 **1 Acknowledgments**  
7

8  
9 2 We are deeply indebted to all of the EMS personnel and concerned physicians in Osaka  
10  
11 3 Prefecture, and the Osaka Medical Association for their indispensable cooperation and  
12  
13 4 generous support. We also thank all members of the Utstein Osaka Project for their  
14  
15 5 contribution in the organization, coordination, and oversight as the steering committee. We  
16  
17 6 also thank BEC SERVICE for English language editing in writing the paper.  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27

28  
29 **8 Contributors**  
30

31  
32 9 All authors (TK, KK, TS, TI, CN, KK, TN, YH, YK, KY, and TS) participated in the study  
33  
34 10 conception and design, acquisition of data, analysis and interpretation of data, drafting the  
35  
36 11 article and revising it critically for important intellectual content, and final approval of the  
37  
38 12 manuscript.  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54

55 **14 Funding**  
56

57  
58 15 This study was supported by a scientific research grant from the Ministry of Health, Labour,  
59  
60 16 and Welfare of Japan (25112601).  
17

18 **Competing interests**

1  
2  
3  
4  
5  
6 1 None.  
7  
8

9 2  
10

11 3 **Ethics approval**

12  
13  
14 4 The study was approved by the institutional review board of Osaka University with the assent  
15  
16  
17 5 of the EMS authorities of the local governments in Osaka Prefecture.  
18  
19

20 6  
21  
22

23 7 **Provenance and peer review**

24  
25  
26 8 Not commissioned; externally peer reviewed.  
27  
28

29 9  
30  
31

32 10 **Data sharing statement**

33  
34  
35 11 TK had full access to all of the data in the study and takes responsibility for the integrity of the  
36  
37  
38 12 data and the accuracy of the data analysis.  
39  
40

41 13  
42  
43

44 14 **Open Access**

45  
46 15 This is an Open Access article distributed in accordance with the Creative Commons  
47  
48  
49 16 Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute,  
50  
51  
52 17 remix, adapt, build upon this work noncommercially, and license their derivative works on  
53  
54  
55 18 different terms, provided the original work is properly cited and the use is non-commercial.  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 See: <http://creativecommons.org/licenses/by-nc/3.0/>  
7  
8

9 2  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

1  
2  
3  
4  
5  
6 **1 REFERENCES**  
7

- 8  
9 2 1. 2010 International consensus on cardiopulmonary resuscitation and emergency  
10  
11  
12 3 cardiovascular care science with treatment recommendations. *Circulation*  
13  
14 4 2010;122:S250-605.
- 15  
16  
17 5 2. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and  
18  
19  
20 6 emergency cardiovascular care. *Circulation* 2010;122:S639-946.
- 21  
22  
23 7 3. European Resuscitation Council Guidelines for Resuscitation 2010. *Resuscitation*  
24  
25  
26 8 2010;81:1219-451.
- 27  
28  
29 9 4. 2010 Japanese guidelines for emergency care and cardiopulmonary resuscitation. 1st ed.  
30  
31  
32 10 Tokyo: Health Shuppansha; 2011 (in Japanese).
- 33  
34  
35 11 5. Iwami T, Nichol G, Hiraide A, *et al.* Continuous improvements of chain of survival  
36  
37  
38 12 increased survival after out-of-hospital cardiac arrests: a large-scale population-based  
39  
40  
41 13 study. *Circulation* 2009;119:728-34.
- 42  
43  
44 14 6. Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation  
45  
46  
47 15 during out-of-hospital ventricular fibrillation arrest: survival implications of guideline  
48  
49  
50 16 changes. *Circulation* 2006;114:2760-5.
- 51  
52  
53 17 7. Kitamura T, Iwami T, Kawamura T, *et al.* Nationwide improvements in survival from  
54  
55  
56 18 out-of-hospital cardiac arrests in Japan. *Circulation* 2012;126:2834-43.
- 57  
58  
59  
60



- 1  
2  
3  
4  
5  
6 1 8. Kitamura T, Iwami T, Kawamura T, *et al.* Bystander-initiated rescue breathing for  
7  
8  
9 2 out-of-hospital cardiac arrests of non-cardiac origin. *Circulation* 2010;122:293-9.  
10  
11  
12 3 9. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin.  
13  
14 4 Epidemiology and outcome. *Eur Heart J* 1997;18:1122-8.  
15  
16  
17 5 10. Engdahl J, Bång A, Karlson BW, *et al.* Characteristics and outcome among patients  
18  
19 6 suffering from out of hospital cardiac arrest of non-cardiac aetiology. *Resuscitation*  
20  
21 7 2003;57:33-41.  
22  
23  
24 8 11. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital  
25  
26 9 cardiac arrest of non-cardiac origin. *Resuscitation* 2007;72:200-7.  
27  
28  
29 10 12. Iwami T, Hiraide A, Nakanishi N, *et al.* Age and sex analyses of out-of-hospital cardiac  
30  
31 11 arrest in Osaka, Japan. *Resuscitation* 2003;57:145-52.  
32  
33  
34 12 13. Engdahl J, Holmberg M, Karlson BW, *et al.* The epidemiology of out-of-hospital ‘sudden’  
35  
36 13 cardiac arrest. *Resuscitation* 2002;52:235-45.  
37  
38  
39 14 14. Cummins RO, Chamberlain DA, Abramson NS, *et al.* Recommended guideline for  
40  
41 15 uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style: a statement  
42  
43 16 for health professionals from a task force of the American Heart Association, the  
44  
45 17 European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the  
46  
47 18 Australian Resuscitation Council. *Circulation* 1991;84:960-75.  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 15. Jacobs I, Nadkarni V, Bahr J, *et al.* Cardiac arrest and cardiopulmonary resuscitation  
7  
8  
9 2 outcome reports: update and simplification of the Utstein templates for resuscitation  
10  
11 3 registries: a statement for healthcare professionals from a task force of the International  
12  
13 4 Liaison Committee on Resuscitation (American Heart Association, European  
14  
15 Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation  
16  
17 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
18  
19 Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.  
20  
21  
22  
23  
24  
25  
26 8 16. Nitta M, Iwami T, Kitamura T, *et al.* Age-specific differences in outcomes after  
27  
28 9 out-of-hospital cardiac arrests. *Pediatrics* 2011;128:e812-20.  
29  
30  
31  
32 10 17. Atkins DL, Everson-Stewart S, Sears GK, *et al.* Epidemiology and outcomes from  
33  
34 11 out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium  
35  
36 12 Epistry-Cardiac Arrest. *Circulation* 2009;119:1484-91.  
37  
38  
39  
40  
41 13 18. 2010 Population Census of Japan.  
42  
43 14 [http://www.stat.go.jp/data/kokusei/2010/index.htm?utm\\_source=twitterfeed&utm\\_mediu](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter)  
44  
45 15 [m=twitter](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter) (Accessed August 05, 2014) (in Japanese).  
46  
47  
48  
49 16 19. Vital Statistics of Japan 2005. Tokyo: Health and Welfare Statistics Association; 2007.  
50  
51  
52 17 20. Hata J, Ninomiya T, Hirakawa Y, *et al.* Secular trends in cardiovascular disease and its  
53  
54 18 risk factors in Japanese: half-century data from the Hisayama Study (1961-2009).  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 *Circulation* 2013;128:1198-205.  
7  
8  
9 2 21. 2011 Overview of Patient Survey. <http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/>  
10  
11  
12 3 (Accessed August 05, 2014) (in Japanese).  
13  
14  
15 4 22. Deasy C, Bray J, Smith K, *et al.* Traumatic out-of-hospital cardiac arrests in Melbourne,  
16  
17  
18 5 Australia. *Resuscitation* 2012;83:465-70.  
19  
20  
21 6 23. Deasy C, Bray J, Smith K, *et al.* Hanging-associated out-of-hospital cardiac arrests in  
22  
23  
24 7 Melbourne, Australia. *Emerg Med J* 2013;30:38-42.  
25  
26  
27 8 24. Hagihara A, Hasegawa M, Abe T, *et al.* Prehospital lactated ringer's solution treatment  
28  
29  
30 9 and survival in out-of-hospital cardiac arrest: a prospective cohort analysis. *PLoS Med*  
31  
32 10 2013;10:e1001394.  
33  
34  
35 11 25. Seymour CW, Cooke CR, Hebert PL, *et al.* Intravenous access during out-of-hospital  
36  
37  
38 12 emergency care of noninjured patients: a population-based outcome study. *Ann Emerg*  
39  
40  
41 13 *Med* 2012;59:296-303.  
42  
43  
44 14 26. Nichol G, Thomas E, Callaway CW, *et al.* Regional variation in out-of-hospital cardiac  
45  
46  
47 15 arrest incidence and outcome. *JAMA* 2008;300:1423-31.  
48  
49  
50 16 27. Neumar RW, Nolan JP, Adrie C, *et al.* Post-cardiac arrest syndrome: epidemiology,  
51  
52  
53 17 pathophysiology, treatment, and prognostication. A Scientific Statement from the  
54  
55  
56 18 International Liaison Committee on Resuscitation; the American Heart Association  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1       Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and  
2  
3  
4  
5  
6  
7  
8  
9       2       Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the  
10  
11  
12       3       Council on Clinical Cardiology; the Council on Stroke. *Circulation* 2008;118:2452-8.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

1  
2  
3  
4  
5  
6 **1 Figure Legends**  
7

8  
9 **2 Figure 1** Overview of EMS-treated cardiac arrests with an abridged Utstein template from  
10  
11  
12 3 January 1, 2005 to December 31, 2011. EMS, emergency medical service.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

**Table 1** Age-adjusted incidences and unadjusted one-month survival rate of out-of-hospital cardiac arrests with non-cardiac origin according to the cause over time

	2005	2006	2007	2008	2009	2010	2011	P for trend
Age-adjusted Incidence per 100,000 persons								
External causes	12.4	12.3	13.2	12.8	13.2	13.3	13.3	0.024
Asphyxia	2.7	3.0	2.8	3.4	3.1	2.9	2.9	0.726
Hanging	3.4	3.4	4.1	3.4	3.7	3.9	3.9	0.158
Fall	2.4	2.5	3.1	2.4	2.9	3.0	2.7	0.396
Drowning	1.2	1.1	1.2	1.4	1.2	1.3	1.6	0.065
Traffic injury	1.6	1.5	1.4	1.4	1.4	1.5	1.4	0.229
Drug overdose	0.5	0.4	0.2	0.4	0.4	0.4	0.3	0.304
Unclassified	0.5	0.5	0.4	0.3	0.5	0.4	0.5	0.447
Respiratory diseases	2.2	1.8	1.8	1.7	1.3	1.3	1.6	0.018
Malignant tumors	1.6	1.8	1.8	1.7	1.5	1.3	1.6	0.109
Strokes	2.0	1.8	1.8	1.6	1.4	1.2	1.3	< 0.001
Others	2.7	3.3	3.1	2.9	2.7	2.5	2.4	0.087
Unadjusted one-month survival, % (n/N)								
External causes	4.8 (53/1100)	6.8 (72/1059)	5.7 (66/1164)	7.2 (85/1184)	7.1 (86/1207)	6.1 (75/1225)	5.6 (73/1300)	0.736
Asphyxia	10.4 (35/337)	15.4 (53/344)	13.0 (44/338)	15.6 (67/430)	16.3 (66/406)	14.8 (58/393)	14.0 (59/422)	0.374
Hanging	4.6 (12/261)	4.7 (12/255)	5 (16/318)	4.8 (13/273)	4.9 (14/287)	3.3 (10/301)	2.3 (7/304)	0.101
Fall	0.6 (1/159)	0.6 (1/169)	0.9 (2/219)	1.2 (2/165)	0.0 (0/197)	0.5 (1/208)	1.1 (2/183)	NA
Drowning	1.3 (2/151)	3.3 (4/120)	0.0 (0/128)	1.3 (2/159)	2.1 (3/144)	0.7 (1/148)	0.0 (0/212)	NA
Traffic injury	0.9 (1/116)	1.0 (1/101)	1.8 (2/109)	0.9 (1/106)	1.9 (2/103)	1.7 (2/115)	2.6 (3/115)	0.027

7	Drug overdose	3.0 (1/33)	0.0 (0/29)	5.6 (1/18)	0.0 (0/25)	3.3 (1/30)	11.1 (3/27)	4.0 (1/25)	NA
8	Unclassified	2.3 (1/43)	2.4 (1/41)	2.9 (1/34)	0.0 (0/26)	0.0 (0/40)	0.0 (0/33)	2.6 (1/39)	NA
10	Respiratory diseases	6.4 (17/267)	3.9 (8/206)	8.0 (17/212)	9.8 (21/214)	6.7 (11/165)	4.7 (8/169)	5.6 (12/215)	0.875
11	Malignant tumors	0.5 (1/186)	0.5 (1/194)	1.0 (2/202)	1.0 (2/196)	0.0 (0/178)	2.5 (4/159)	0.5 (1/194)	NA
12	Strokes	3.6 (7/196)	6.1 (11/179)	4.5 (8/176)	3.2 (5/154)	4.9 (7/143)	6.0 (8/134)	6.8 (9/132)	0.241
14	Others	2.9 (8/277)	7.0 (22/314)	1.3 (4/308)	4.5 (14/311)	4.3 (12/278)	5.3 (15/281)	3.5 (10/285)	0.808

16 NA indicates not analyzed.

**Table 2** Patient and EMS characteristics of out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n=14,164)	External causes (n = 8239)	Respiratory diseases (n=1448)	Malignant tumors (n=1309)	Strokes (n=1114)	Others (n =2054)	<i>P</i> value*
Age, yr, mean (SD)	66.8 (19.0)	63.5 (20.5)	76.1 (14.2)	71.9 (12.0)	67.7 (14.7)	69.8 (17.6)	< 0.001
Age group, n (%)							< 0.001
Adults aged 20-64 years	5513 (38.9)	3826 (46.4)	229 (15.8)	345 (26.4)	447 (40.1)	666 (32.4)	
Elderly aged >=65 years	8651 (61.1)	4413 (53.6)	1219 (84.2)	964 (73.6)	667 (59.9)	1388 (67.6)	
Men, n (%)	8215 (58.0)	4789 (58.1)	844 (58.3)	881 (67.3)	559 (50.2)	1142 (55.6)	< 0.001
Arrests witnessed by bystanders, n (%)	5561 (39.3)	2952 (35.8)	682 (47.1)	639 (48.8)	493 (44.3)	795 (38.7)	< 0.001
Good activities of daily living, n (%)	8522 (60.2)	5213 (63.3)	653 (45.1)	443 (33.8)	896 (80.4)	1317 (64.1)	< 0.001
First documented rhythm, n (%)							< 0.001
VF	324 (2.3)	119 (1.4)	35 (2.4)	26 (2.0)	69 (6.2)	75 (3.7)	
PEA	3356 (23.7)	1853 (22.5)	394 (27.2)	262 (20.0)	329 (29.5)	518 (25.2)	
Asystole	10196 (72.0)	6124 (74.3)	983 (67.9)	1008 (77.0)	647 (58.1)	1434 (69.8)	
Others	288 (2.0)	143 (1.7)	36 (2.5)	13 (1.0)	69 (6.2)	27 (1.3)	
Location of arrest, n (%)							< 0.001
Homes	9010 (63.6)	4435 (53.8)	1098 (75.8)	1217 (93.0)	801 (71.9)	1459 (71.0)	
Public places	2035 (14.4)	1608 (19.5)	59 (4.1)	24 (1.8)	156 (14.0)	188 (9.2)	
Work places	346 (2.4)	223 (2.7)	7 (0.5)	4 (0.3)	48 (4.3)	64 (3.1)	
Health care facilities	1505 (10.6)	904 (11.0)	248 (17.1)	55 (4.2)	63 (5.7)	235 (11.4)	
Others	1268 (9.0)	1069 (13.0)	36 (2.5)	9 (0.7)	46 (4.1)	108 (5.3)	
Public-access AED use, n (%)	13 (0.1)	4 (0.05)	2 (0.1)	0 (0.0)	5 (0.4)	2 (0.1)	0.001
Type of Bystander CPR, n (%)							< 0.001
No CPR	9023 (63.7)	5383 (65.3)	836 (57.7)	889 (67.9)	633 (56.8)	1282 (62.4)	
Chest compression-only CPR	3288 (23.2)	1811 (22.0)	408 (28.2)	297 (22.7)	283 (25.4)	489 (23.8)	



Conventional CPR with rescue breathing	1853 (13.1)	1045 (12.7)	204 (14.1)	123 (9.4)	198 (17.8)	283 (13.8)	
Intravascular fluid, n (%)	2320 (16.4)	1458 (17.7)	202 (14.0)	113 (8.6)	230 (20.6)	317 (15.4)	< 0.001
Intubation, n (%)	2639 (18.6)	1364 (16.6)	338 (23.3)	242 (18.5)	257 (23.1)	438 (21.3)	< 0.001
Epinephrine, n (%)	987 (7.0)	572 (6.9)	88 (6.1)	49 (3.7)	125 (11.2)	153 (7.4)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.9 (4.1)	8.0 (4.6)	7.7 (3.0)	7.7 (2.7)	7.7 (2.8)	7.9 (3.8)	0.003
Call to CPR by EMS, min, mean (SD)	8.5 (4.5)	8.8 (5.1)	8.1 (3.1)	8.1 (2.8)	8.2 (2.9)	8.4 (4.2)	< 0.001
Call to hospital arrival, min, mean (SD)	28.2 (8.6)	28.4 (8.6)	27.3 (8.2)	28.0 (8.9)	28.2 (8.4)	28.1 (8.7)	0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

Data on the times from call to contact with a patient, CPR by EMS, and hospital arrival were missing for 33, 40, and 166 victims, respectively.

**Table 3** Patient and EMS characteristics of out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Age, yr, mean (SD)	77.9 (14.4)	55.6 (17.4)	47.4 (17.4)	73.1 (14.8)	52.6 (19.0)	49.9 (19.5)	58.1 (19.3)	< 0.001
Age group, n (%)								< 0.001
Adults aged 20-64 years	403 (15.1)	1136 (66.8)	1055 (81.2)	210 (19.8)	523 (68.4)	141 (75.4)	158 (61.7)	
Elderly aged ≥65 years	2267 (84.9)	663 (33.2)	245 (18.8)	852 (80.2)	242 (31.6)	46 (24.6)	98 (38.3)	
Men, n (%)	1345 (50.4)	1290 (64.5)	781 (60.1)	530 (49.9)	558 (72.9)	117 (62.6)	168 (65.6)	< 0.001
Arrests witnessed by bystanders, n (%)	1801 (67.5)	27 (1.4)	510 (39.2)	56 (5.3)	476 (62.2)	10 (5.3)	72 (28.1)	< 0.001
Good activities of daily living, n (%)	1099 (41.2)	1769 (88.5)	685 (52.7)	854 (80.4)	517 (67.6)	133 (71.1)	156 (60.9)	< 0.001
First documented rhythm, n (%)								< 0.001
VF	56 (2.1)	13 (0.7)	19 (1.5)	12 (1.1)	14 (1.8)	1 (0.5)	4 (1.6)	
PEA	960 (36.0)	198 (9.9)	274 (21.1)	72 (6.8)	259 (33.9)	20 (10.7)	70 (27.3)	
Asystole	1589 (59.5)	1775 (88.8)	985 (75.8)	970 (91.3)	469 (61.3)	160 (85.6)	176 (68.8)	
Others	65 (2.4)	13 (0.7)	22 (1.7)	8 (0.8)	23 (3.0)	6 (3.2)	6 (2.3)	
Location of arrest, n (%)								< 0.001
Homes	1596 (59.8)	1667 (83.4)	139 (10.7)	770 (72.5)	2 (0.3)	150 (80.2)	111 (43.4)	
Public places	139 (5.2)	86 (4.3)	553 (42.5)	83 (7.8)	677 (88.5)	14 (7.5)	56 (21.9)	
Workplaces	35 (1.3)	94 (4.7)	44 (3.4)	3 (0.3)	7 (0.9)	7 (3.7)	33 (12.9)	
Health care facilities	835 (31.3)	27 (1.4)	12 (0.9)	14 (1.3)	1 (0.1)	0 (0.0)	15 (5.9)	
Others	65 (2.4)	125 (6.3)	552 (42.5)	192 (18.1)	78 (10.2)	16 (8.6)	41 (16.0)	

Public-access AED use, n (%)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.214
Type of Bystander CPR, n (%)									< 0.001
No CPR	1386 (51.9)	1174 (58.7)	1191 (91.6)	608 (57.3)	673 (88.0)	154 (82.4)	197 (77.0)		
Chest compression-only CPR	748 (28.0)	549 (27.5)	93 (7.2)	281 (26.5)	74 (9.7)	23 (12.3)	43 (16.8)		
Conventional CPR with rescue breathing	536 (20.1)	276 (13.8)	16 (1.2)	173 (16.3)	18 (2.4)	10 (5.3)	16 (6.2)		
Intravascular fluid, n (%)	540 (20.2)	393 (19.7)	107 (8.2)	281 (26.5)	76 (9.9)	27 (14.4)	34 (13.3)	< 0.001	
Intubation, n (%)	800 (30.0)	167 (8.4)	41 (3.2)	251 (23.6)	31 (4.1)	33 (17.6)	41 (16.0)	< 0.001	
Epinephrine, n (%)	326 (12.2)	83 (4.2)	41 (3.2)	68 (6.4)	37 (4.8)	6 (3.2)	11 (4.3)	< 0.001	
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.6 (2.9)	7.8 (3.3)	7.4 (3.3)	9.4 (7.6)	7.6 (4.2)	14.2 (10.7)	9.4 (7.3)	< 0.001	
Call to CPR by EMS personnel, min, mean (SD)	7.9 (3.1)	8.6 (3.9)	8.2 (3.8)	10.0 (7.5)	9.3 (5.9)	14.4 (10.0)	11.0 (8.7)	< 0.001	
Call to hospital arrival, min, mean (SD)	28.6 (8.6)	28.2 (7.9)	27.5 (8.3)	29.1 (9.3)	27.1 (8.8)	32.1 (11.1)	29.5 (9.4)	< 0.001	

\*P values are calculated to test the homogeneity among the 7 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

**Table 4** Outcomes after out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 1,4164)	External causes (n = 8239)	Respiratory diseases (n = 1448)	Malignant tumors (n = 1309)	Strokes (n = 1114)	Others (n =2054)	<i>P</i> value *
Prehospital ROSC, n (%)	1229 (8.7)	703 (8.5)	114 (7.9)	57 (4.4)	216 (19.4)	139 (6.8)	< 0.001
Total ROSC, n (%)	4744 (33.5)	2638 (32.0)	620 (42.8)	234 (17.9)	650 (58.3)	602 (29.3)	< 0.001
Hospital admission, n (%)	4142 (29.2)	2356 (28.6)	530 (36.6)	173 (13.2)	585 (52.5)	498 (24.2)	< 0.001
One-month survival, n (%)	755 (5.3)	510 (6.2)	94 (6.5)	11 (0.8)	55 (4.9)	85 (4.1)	< 0.001
Neurologically favorable outcome, n (%)	188 (1.3)	105 (1.3)	27 (1.9)	2 (0.2)	17 (1.5)	37 (1.8)	< 0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

ROSC indicates return of spontaneous circulation.

Data on one-month survival and neurological status were missing for 7 victims.

**Table 5** Outcomes after out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Prehospital ROSC, n (%)	463 (17.3)	144 (7.2)	22 (1.7)	36 (3.4)	28 (3.7)	4 (2.1)	6 (2.3)	< 0.001
Total ROSC, n (%)	1003 (37.6)	1500 (75.0)	1213 (93.3)	894 (84.2)	637 (83.3)	143 (76.5)	211 (82.4)	< 0.001
Hospital admission, n (%)	1529 (57.3)	453 (22.7)	62 (4.8)	147 (13.8)	92 (12.0)	40 (21.4)	33 (12.9)	< 0.001
One-month survival, n (%)	382 (14.3)	84 (4.2)	9 (0.7)	12 (1.1)	12 (1.6)	7 (3.7)	4 (1.6)	< 0.001
Neurologically favorable outcome, n (%)	71 (2.7)	17 (0.9)	1 (0.1)	4 (0.4)	6 (0.8)	4 (2.1)	2 (0.8)	< 0.001

\**P* values are calculated to test the homogeneity among the 7 cause groups.

ROSC indicates return of spontaneous circulation.

**Table 6** Factors associated with outcomes after out-of-Hospital cardiac arrests with non-cardiac origin

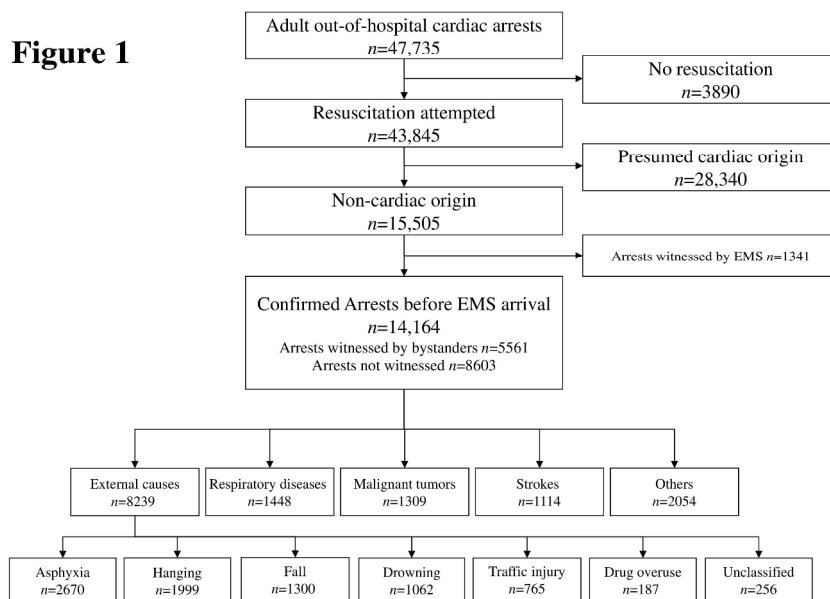
	One-month survival				Neurologically favorable outcome			
	Crude OR	(95% CI)	Adjusted OR	(95% CI)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	0.95	(0.82-1.10)	1.36	(1.12-1.65)	1.02	(0.76-1.37)	1.52	(1.07-2.15)
Men	0.75	(0.64-0.88)	0.99	(0.84-1.16)	1.09	(0.81-1.46)	0.91	(0.67-1.24)
Witnessed by bystanders	4.41	(3.74-5.19)	4.13	(3.35-5.09)	4.48	(3.23-6.21)	4.83	(3.21-7.29)
Good activities of daily living	0.93	(0.80-1.08)	1.23	(1.03-1.47)	1.39	(1.02-1.88)	1.43	(1.02-2.02)
VF	2.74	(1.96-3.82)	2.04	(1.42-2.92)	7.72	(5.05-11.79)	5.40	(3.40-8.59)
Type of bystander CPR								
No CPR	Reference		Reference		Reference		Reference	
Chest compression-only CPR	0.97	(0.81-1.16)	0.80	(0.66-0.98)	0.95	(0.67-1.35)	0.92	(0.64-1.33)
Conventional CPR with rescue breathing	1.47	(1.20-1.79)	1.07	(0.86-1.34)	1.01	(0.65-1.55)	0.89	(0.56-1.42)
Type of non-cardiac origin								
Respiratory diseases	0.42	(0.33-0.53)	0.51	(0.40-0.65)	0.70	(0.44-1.09)	0.76	(0.48-1.21)
Malignant tumors	0.05	(0.03-0.09)	0.06	(0.03-0.11)	0.06	(0.01-0.23)	0.06	(0.01-0.23)
Strokes	0.31	(0.23-0.42)	0.27	(0.20-0.38)	0.57	(0.33-0.97)	0.34	(0.19-0.61)
Asphyxia	Reference		Reference		Reference		Reference	
Hanging	0.26	(0.21-0.34)	0.56	(0.41-0.77)	0.31	(0.18-0.53)	0.55	(0.28-1.07)
Fall	0.04	(0.02-0.08)	0.03	(0.01-0.06)	0.03	(0.004-0.20)	0.01	(0.002-0.11)
Drowning	0.07	(0.04-0.12)	0.16	(0.09-0.29)	0.14	(0.05-0.38)	0.31	(0.11-0.90)

Traffic injury	0.10 (0.05-0.17)	0.05 (0.03-0.10)	0.29 (0.13-0.67)	0.10 (0.04-0.26)
Drug overdose	0.23 (0.11-0.50)	0.58 (0.26-1.29)	0.80 (0.29-2.21)	1.74 (0.58-5.19)
Others	0.26 (0.20-0.33)	0.29 (0.22-0.38)	0.67 (0.45-1.00)	0.60 (0.39-0.92)
Unclassified	0.10 (0.04-0.26)	0.10 (0.04-0.28)	0.29 (0.07-1.18)	0.27 (0.06-1.16)
Location of arrest				
Homes	Reference	Reference	Reference	Reference
Public places	0.78 (0.61-0.99)	1.45 (1.10-1.91)	1.11 (0.75-1.65)	1.54 (0.97-2.44)
Workplaces	1.29 (0.83-1.98)	1.40 (0.87-2.23)	1.26 (0.55-2.89)	0.95 (0.39-2.30)
Health care facilities	1.69 (1.38-2.07)	0.88 (0.69-1.12)	0.72 (0.42-1.24)	0.47 (0.26-0.85)
Others	0.70 (0.51-0.94)	1.67 (1.19-2.35)	0.68 (0.38-1.24)	1.35 (0.72-2.54)
Intravascular fluid	1.78 (1.50-2.11)	1.45 (1.14-1.84)	1.34 (0.94-1.91)	1.52 (0.97-2.38)
Intubation	1.62 (1.37-1.92)	1.02 (0.84-1.23)	0.73 (0.48-1.10)	0.50 (0.32-0.77)
Epinephrine	2.32 (1.87-2.88)	0.97 (0.71-1.32)	1.25 (0.74-2.09)	0.60 (0.31-1.17)
EMS response time (for one-increment of minute)	0.93 (0.91-0.96)	0.92 (0.90-0.95)	0.91 (0.86-0.96)	0.90 (0.84-0.95)
Year (for one-increment of year)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.02 (0.95-1.09)	1.05 (0.97-1.13)

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**Figure 1**



297x209mm (300 x 300 DPI)

view only



**Supplemental Table** Factors associated with one-month survival after out-of-hospital cardiac arrests with non-cardiac origin by internal and external causes

	One-month survival			
	Internal causes		External causes	
	Adjusted OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	1.01	(0.68 - 1.50)	1.51	(1.17 - 1.96)
Men	0.99	(0.71 - 1.40)	0.91	(0.75 - 1.11)
Witnessed by bystanders	2.86	(1.99 - 4.11)	5.03	(3.71 - 6.81)
Good activities of daily living	1.27	(0.87 - 1.85)	1.34	(1.08 - 1.67)
VF	2.35	(1.30 - 4.24)	0.44	(0.17 - 1.11)
Type of bystander CPR				
No CPR	Reference		Reference	
Chest compression-only CPR	0.66	(0.43 - 1.01)	0.79	(0.61 - 1.01)
Conventional CPR with rescue breathing	0.83	(0.51 - 1.36)	1.18	(0.89 - 1.54)
Type of non-cardiac origin				
Respiratory diseases	Reference		--	
Malignant tumors	0.12	(0.06 - 0.23)	--	
Strokes	0.55	(0.37 - 0.82)	--	
Asphyxia	--		Reference	
Hanging	--		0.60	(0.41 - 0.87)
Fall	--		0.03	(0.01 - 0.06)
Drowning	--		0.05	(0.03 - 0.11)
Traffic injury	--		0.17	(0.09 - 0.31)
Drug overdose	--		0.60	(0.26 - 1.36)
Location of arrest				
Homes	Reference		Reference	
Public places	2.01	(1.21 - 3.36)	1.39	(0.94 - 2.04)
Workplaces	1.88	(0.69 - 5.15)	1.47	(0.77 - 2.80)
Health care facilities	1.00	(0.55 - 1.81)	0.82	(0.62 - 1.09)
Others	2.10	(0.99 - 4.47)	1.72	(1.12 - 2.63)
Intravascular fluid	0.65	(0.33 - 1.29)	1.69	(1.27 - 2.25)
Intubation	0.62	(0.39 - 0.97)	1.21	(0.96 - 1.52)
Epinephrine	1.89	(0.82 - 4.34)	0.93	(0.64 - 1.35)
EMS response time (for one-increment of minute)	0.97	(0.91 - 1.03)	0.93	(0.90 - 0.96)
Year (for one-increment of year)	1.02	(0.94 - 1.11)	1.01	(0.96 - 1.06)

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

1 **Epidemiology and outcome of adult out-of-hospital cardiac arrest**  
2 **with non-cardiac origin in Osaka: a population-based study**

3  
4 Tetsuhisa Kitamura,<sup>1</sup> Kosuke Kiyohara,<sup>2</sup> Tomohiko Sakai,<sup>3</sup> Taku Iwami,<sup>4</sup> Chika Nishiyama,<sup>5</sup>  
5 Kentaro Kajino,<sup>6</sup> Tatsuya Nishiuchi,<sup>7</sup> Yasuyuki Hayashi,<sup>8</sup> Yusuke Katayama,<sup>3</sup> Kazuhisa  
6 Yoshiya,<sup>3</sup> Takeshi Shimazu<sup>3</sup>

7  
8 **Author affiliations**

9 <sup>1</sup>Division of Environmental Medicine and Population Sciences, Department of Social and  
10 Environmental Medicine, Graduate School of Medicine, Osaka University, Japan

11 <sup>2</sup>Department of Public Health, Tokyo Women's Medical University, Japan

12 <sup>3</sup>Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School  
13 of Medicine, Japan

14 <sup>4</sup>Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto, Japan

15 <sup>5</sup>Department of Critical Care Nursing, Graduate School of Medicine and School of Health  
16 Sciences, Kyoto University, Japan

17 <sup>6</sup>Traumatology and Critical Care Medical Center, National Hospital Organization Osaka  
18 National Hospital, Japan

1  
2  
3  
4  
5  
6 1 <sup>7</sup>Department of Acute Medicine, Kinki University Faculty of Medicine, Japan  
7  
8

9 2 <sup>8</sup>Senri Critical Care Medical Center, Osaka Saiseikai Senri Hospital, Japan  
10  
11  
12 3  
13

14 **Correspondence to**

15 Taku Iwami MD, PhD  
16  
17  
18

19  
20  
21 6 Kyoto University Health Services, Yoshida-Honmachi, Sakyo-ku, Kyoto 606-8501  
22  
23

24 7 Phone: +81-75-753-2426; Fax: +81-75-753-2424  
25  
26

27 8 E-mail: iwamit@e-mail.jp  
28  
29  
30  
31

32 10 **Total word count:** 2857 words (main text). **Abstract:** 285 words.  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

11

1  
2  
3  
4  
5  
6 **1 ABSTRACT**

7  
8  
9 **2 Objectives:** To evaluate epidemiological characteristics of out-of-hospital cardiac  
10  
11  
12 **3 arrests (OHCAs)** by detailed non-cardiac cause and factors associated with the  
13  
14  
15 **4 outcomes** after OHCAs with non-cardiac origin.

16  
17  
18 **5 Design:** A prospective, population-based observational study.

19  
20  
21 **6 Setting:** The Utstein Osaka Project.

22  
23 **7 Participants:** 14,164 adult patients aged  $\geq 20$  years old with OHCAs due to  
24  
25  
26 **8 non-cardiac** origin who were resuscitated by emergency-medical-service personnel or  
27  
28  
29 **9 bystanders**, and then were transported to medical institutions from January 2005 to  
30  
31  
32 **10 December** 2011.

33  
34  
35 **11 Primary outcome measures:** One-month survival after OHCA. Multiple logistic  
36  
37  
38 **12 regression** analysis was used to assess factors that were potentially associated with the  
39  
40  
41 **13 outcome**.

42  
43  
44 **14 Results:** During the study period, the one-month survival rate was 5.3% (755/14,164).

45  
46  
47 **15 The** proportion of one-month survival was 6.2% (510/8239) in external causes, 6.5%  
48  
49  
50 **16 (94/1148)** in respiratory diseases, 0.8% (11/1309) in malignant tumors, 4.9% (55/1114)  
51  
52  
53 **17 in** strokes, and 4.1% (85/2054) in others. As for external causes, the proportion of  
54  
55  
56 **18 one-month** survival was 14.3% (382/2670) in asphyxia, 4.2% (84/1999) in hanging,

1 0.7% (9/1300) in fall, 1.1% (12/1062) in drowning, 1.6% (12/765) in traffic injury,  
2 3.7% (7/187) in drug overuse, and 1.6% (4/256) in unclassified external causes. In a  
3 multivariate analysis, adults aged <65 years old, arrests witnessed by bystanders, good  
4 activities of daily living before arrests, ventricular fibrillation arrests, public places,  
5 intravenous fluid, and early emergency-medical-service response time were significant  
6 predictors for one-month outcome after OHCA with non-cardiac origin. The  
7 proportion of one-month survival of the whole OHCA with non-cardiac origin did not  
8 significantly increase (from 4.3% [86/2023] in 2005 to 4.9% [105/2126] in 2011) and  
9 the adjusted odds ratio for one-increment of year was 1.01 (95% confidence interval  
10 0.97-1.06).

11 **Conclusions:** From a large OHCA registry in Osaka, we demonstrated that one-month  
12 survival after OHCA with non-cardiac origin was poor and stable.

13

1  
2  
3  
4  
5  
6 **1 Strengths and limitations of this study**  
7

8  
9 ■ This study showed that one-month survival after OHCA with non-cardiac origin  
10  
11 was poor and the survival trends did not improve year-by-year in Osaka during the  
12  
13 study period from 2005 to 2011. In addition, the survival rates differed by  
14  
15 detailed non-cardiac origin.  
16  
17  
18

19  
20 ■ The category of presumed non-cardiac causes is made clinically, as per the  
21  
22 Utstein-style international guidelines for cardiac arrest data reporting.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 INTRODUCTION

2 Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in the  
3 industrialized world.<sup>1-4</sup> Although improvements in the chain of survival including the  
4 development of a public-access defibrillation system and revisions to cardiopulmonary  
5 resuscitation (CPR) guidelines have led to increased survival after OHCA with cardiac  
6 origin in some communities,<sup>5-7</sup> the outcome after OHCA with non-cardiac origin  
7 remains generally poor.<sup>7-13</sup>

8 Importantly, 20% to 40% of adult OHCA were reportedly of non-cardiac origin.<sup>7-13</sup>  
9 However, epidemiological characteristics of OHCA with non-cardiac origin have not  
10 been sufficiently investigated as much as those of OHCA with cardiac origin.  
11 Therefore, the evaluation of characteristics, trends, and outcomes by detailed  
12 non-cardiac cause and understanding the factors associated with the outcomes are  
13 needed to improve the survival after OHCA with non-cardiac origin.

14 The Utstein Osaka Project is a large prospective population-based cohort study of  
15 OHCA in Osaka, Japan, covering about 8.8 million residents.<sup>5</sup> During the 7 years from  
16 2005 to 2011, we enrolled approximately 14,000 OHCA with non-cardiac origin  
17 before emergency-medical-service (EMS) arrival. The present study aimed to evaluate  
18 the epidemiological characteristics of OHCA by detailed non-cardiac cause. In

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 addition, we evaluated factors associated with the outcomes after OHCA with  
2 non-cardiac origin in a multivariate analysis.  
3

For peer review only



1  
2  
3  
4  
5  
6 **1 METHODS**

7  
8  
9 **2 Study design and setting**

10  
11  
12 3 The Utstein Osaka Project is a prospective, population-based registry of OHCA that is  
13  
14 4 based on the standardized Utstein style.<sup>14,15</sup> This study enrolled adult patients aged  
15  
16  
17 5 =>20 years suffering OHCAs with non-cardiac origin before EMS arrival, who were  
18  
19  
20 6 resuscitated by EMS personnel or bystanders, and were transported to medical  
21  
22  
23 7 institutions in Osaka Prefecture from January 1, 2005 to December 31, 2011. In this  
24  
25  
26 8 study, we excluded pediatric OHCA patients because characteristics and outcomes  
27  
28  
29 9 from OHCAs differed between children and adults.<sup>16,17</sup>

30  
31  
32 10 Cardiac arrest was defined as the cessation of cardiac mechanical activity as  
33  
34  
35 11 confirmed by the absence of signs of circulation.<sup>14,15</sup> In this study, the arrests were  
36  
37  
38 12 classified into those of presumed cardiac origin and non-cardiac origin, the latter  
39  
40  
41 13 resulting from external causes, respiratory diseases, malignant tumors, strokes, and any  
42  
43  
44 14 other non-cardiac causes based on hospital medical records. Furthermore, external  
45  
46  
47 15 causes were divided into the seven categories: asphyxia, hanging, fall, drowning,  
48  
49  
50 16 traffic injury, drug overuse, and unclassified external causes. These diagnoses were  
51  
52  
53 17 made clinically by the physician in charge, working in collaboration with the EMS  
54  
55  
56 18 personnel.

1

## 2 EMS organization in Osaka

3 Details of the EMS system in Osaka were described previously.<sup>5</sup> Osaka is the second  
4 largest prefecture in Japan with a population of approximately 8.8 million inhabitants  
5 in an area of 1892 km<sup>2</sup>. In Osaka, there are 34 fire stations with emergency dispatch  
6 centers. The EMS system is operated by the local fire stations. When called, an  
7 ambulance is dispatched from the nearest fire station. Emergency services are provided  
8 24 hours each day by them, which is single-tiered in 32 stations and two-tiered in two  
9 stations. The latter uses medics followed by physicians.

10 Most highly-trained prehospital emergency care providers are called Emergency  
11 Life-Saving Technicians (ELSTs). Usually, each ambulance has a crew of three  
12 emergency providers including at least one ELST. They were allowed to insert an  
13 intravenous line and an adjunct airway, and to use a semi-automated external  
14 defibrillator for OHCA patients. Specially trained ELSTs were permitted to tracheal  
15 intubation since July 2004 and administer intravenous epinephrine since April 2006.

16 Do-not-resuscitate (DNR) orders or living wills are not generally accepted in Japan.  
17 EMS providers are not permitted to terminate resuscitation in the field. Therefore,  
18 almost patients with OHCA who were treated by EMS personnel were transported to a

1 hospital and enrolled in the Utstein Osaka Project, excluding those with decapitation,  
2 incineration, decomposition, rigor mortis, or dependent cyanosis.

#### 3 4 **CPR and AED training for the general public**

5 The use of an automated external defibrillator (AED) by citizens was permitted legally  
6 in July 2004. In Osaka, approximately 14,000 citizens per year participated in the CPR  
7 training programs, consisting of conventional CPR including chest compressions,  
8 mouth-to-mouth ventilation, and AED usage by local fire departments, the Japan Red  
9 Cross, Inc., and the Osaka Life Support Association.<sup>5</sup> All EMS providers perform CPR  
10 according to the Japanese CPR guidelines.<sup>4</sup>

#### 11 12 **Data collection and quality control**

13 Data collection were prospectively conducted using a form that included data  
14 recommended in the Utstein-style reporting guidelines for cardiac arrests.<sup>14,15</sup> These  
15 data included gender, age, first documented cardiac rhythm, witness status, location of  
16 arrests, activity of daily living (ADL) before arrests, time-courses of resuscitation, type  
17 of bystander-initiated CPR, public-access AED use, intravascular fluid, tracheal  
18 intubation, and intravascular epinephrine as well as prehospital return of spontaneous

1  
2  
3  
4  
5  
6 1 circulation (ROSC), total ROSC, one-month survival, and neurological status one  
7  
8  
9 2 month after the event. First documented rhythm was recorded and diagnosed by the  
10  
11  
12 3 EMS personnel with semi-automated defibrillators on the scene, and confirmed by the  
13  
14  
15 4 physician who was responsible for the on-line medical direction. Bystander CPR  
16  
17  
18 5 included chest compression-only CPR and conventional CPR with rescue breathing. A  
19  
20  
21 6 series of EMS times of call receipt, vehicle arrival at the scene, contact with patients,  
22  
23  
24 7 initiation of CPR, defibrillation by EMS, and hospital arrival were recorded  
25  
26  
27 8 automatically at the dispatch center.

28  
29 9 The data form was completed by the EMS personnel in cooperation with the  
30  
31  
32 10 physicians in charge of the patients, and the data were integrated into the registry  
33  
34  
35 11 system on the Information Center for Emergency Medical Services of Osaka, and then  
36  
37  
38 12 checked by the investigators. If the data sheet was incomplete, the relevant EMS  
39  
40  
41 13 personnel were contacted and questioned for data completion.

42  
43  
44 14 All survivors suffering OHCA were followed up for up to one-month after the event  
45  
46  
47 15 by the EMS personnel in charge. One-month neurological outcomes were determined  
48  
49  
50 16 by the physician responsible for treating the patient, using the cerebral performance  
51  
52  
53 17 category (CPC) scale: category 1, good cerebral performance; category 2, moderate  
54  
55  
56 18 cerebral disability; category 3, severe cerebral disability; category 4, coma or  
57  
58  
59  
60

1 vegetative state; and category 5, death.<sup>14,15</sup>

2

### 3 **Outcome measures**

4 The main outcome measure was one-month survival. Secondary outcome measures  
5 included prehospital and total ROSCs, admission to hospital, and one-month survival  
6 with neurologically favorable outcome. Neurologically favorable outcome was defined  
7 as CPC category 1 or 2.<sup>14,15</sup>

8

### 9 **Statistical analysis**

10 In this study, patient and EMS characteristics of OHCAs with non-cardiac origin and  
11 their outcomes were compared between the groups using unpaired analysis of variance  
12 for numerical variables, and chi-square test or Fisher's exact test for categorical  
13 variables by cause of arrest. First, non-cardiac causes were divided into the following  
14 five groups; external causes, respiratory diseases, malignant tumors, strokes, and any  
15 other non-cardiac causes. Next, external causes were further divided into asphyxia,  
16 hanging, fall, drowning, traffic injury, drug overuse, and unclassified external causes.  
17 Age-adjusted annual incidence of OHCAs by non-cardiac origin was calculated by the  
18 direct method using 2005 census data and 1985 Japanese model population.<sup>18,19</sup>

1  
2  
3  
4  
5  
6 1 Poisson regression models for the trends in the incidence and one-month survival rate  
7  
8  
9 2 were used. Multiple logistic regression analysis assessed the factors associated with  
10  
11  
12 3 one-month survival and neurological favorable outcome, and adjusted odds ratios  
13  
14 4 (AORs) and their 95% confidence intervals (CIs) were calculated. As potential  
15  
16  
17 5 confounders, factors that were biologically essential and considered to be associated  
18  
19  
20 6 with clinical outcomes were taken in the multivariable analyses.<sup>7</sup> These variables  
21  
22  
23 7 included age (20-64, ≥65 years old), gender (men, women), witness status (none,  
24  
25  
26 8 witnessed by bystanders), ADL before arrests (good, other), first documented rhythm  
27  
28  
29 9 (VF, non-VF), bystander CPR status (none, compression-only CPR, conventional CPR),  
30  
31  
32 10 type of non-cardiac causes (the 11 categories described above), location of arrests  
33  
34  
35 11 (homes, public places, work places, health care facilities, others), intravascular fluid  
36  
37  
38 12 (yes, no), intubation (yes, no), epinephrine (yes, no), EMS response time (call to  
39  
40  
41 13 contact with patients), and year of arrest. In addition, we conducted a multivariate  
42  
43  
44 14 analysis of one-month survival from OHCA with non-cardiac origin after dividing the  
45  
46  
47 15 two groups: internal (respiratory diseases, malignant tumors, and strokes) and external  
48  
49  
50 16 (asphyxia, hanging, fall, drowning, traffic injury, and drug overuse) causes.

51  
52  
53 17 All statistical analyses were performed using the SPSS statistical package ver21.0J  
54  
55  
56 18 (IBM Corp. Armonk, NY). All of the tests were 2-tailed and *P* values of <0.05 were  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 considered statistically significant.  
7  
8  
9 2  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## 1 RESULTS

2 Figure 1 shows an overview of the study patients based on the Utstein template. A total  
3 of 47,735 adult arrests were documented during these seven years. Resuscitation was  
4 attempted in 43,845, and 15,505 of them were of non-cardiac origin. Excluding 1341  
5 victims who were witnessed by EMS (arrests after EMS arrival), 14,164 (5561 in  
6 bystander-witnessed cases and 8603 in non-witnessed cases) were eligible for our  
7 analyses. Among these arrests, 8239 (58.2%) were due to external causes, 1448  
8 (10.2%) respiratory diseases, 1309 (9.2%) malignant tumors, 1114 (7.9%) strokes, and  
9 2054 (14.5%) others. Among external causes, 2670 (16.5%) were of asphyxia, 1999  
10 (14.1%) hanging, 1300 (9.2%) fall, 1062 (7.5%) drowning, 765 (5.4%) traffic injury,  
11 and 256 (1.8%) unclassified external cause. We could not obtain information on  
12 one-month survival and neurological status for 7 (0.05%) among 14,164 eligible  
13 victims.

14 The age-adjusted annual incidence rates per 100,000 persons by non-cardiac cause  
15 were calculated over time (Table 1). The incidence rate of OHCA with external  
16 causes significantly increased from 12.4 in 2005 to 13.3 in 2011 (P for trend=0.024).  
17 The incidence rate significantly decreased among OHCA patients with respiratory  
18 diseases (from 2.2 in 2005 to 1.6 in 2011, P for trend=0.018) and strokes (from 2.0 in



1  
2  
3  
4  
5  
6 1 2005 to 1.3 in 2011, P for trend<0.001). The unadjusted one-month survival rates by  
7  
8  
9 2 non-cardiac cause were almost stable during the study period.

10  
11 Patient and EMS characteristics of OHCAs with non-cardiac origin according to the  
12  
13 cause are shown in Table 2, and their outcomes in Table 4. The mean age of all OHCA  
14  
15 patients with non-cardiac origin was 66.8 years and males were 58.0%. The proportion  
16  
17 of bystander-witnessed arrests, ADL before arrests, first documented rhythm, type of  
18  
19 bystander CPR, and advanced life supports such as intravascular fluid, intubation, and  
20  
21 epinephrine exceedingly varied between the five groups. In the whole patients, the rate  
22  
23 of one-month survival and neurologically favorable outcome was 5.3% and 1.3%. The  
24  
25 proportion of one-month survival was 6.2% in external causes, 6.5% in respiratory  
26  
27 diseases, 0.8% in malignant tumors, 4.9% in strokes, and 4.1% in others. Furthermore,  
28  
29 patient and EMS characteristics of OHCAs in external causes are shown in Table 3,  
30  
31 and their outcomes in Table 5. The characteristics and outcomes varied between the  
32  
33 seven groups. The proportion of one-month survival was 14.3% in asphyxia, 4.2% in  
34  
35 hanging, 0.7% in fall, 1.1% in submersion, 1.6% in traffic injury, 3.7% in drug overuse,  
36  
37 and 1.6% in unclassified external cause. The proportion of bystander chest  
38  
39 compression-only CPR and conventional CPR with rescue breathing was 23.2% and  
40  
41 13.1% in whole OHCAs with non-cardiac origin, and 22.1% and 14.3% in  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 bystander-witnessed OHCAs.

2 Table 6 shows factors contributing to one-month survival and neurologically  
3 favorable outcome after OHCAs with non-cardiac origin. In one-month survival, adults  
4 aged <65 years old (AOR 1.36, 95% CI 1.12-1.65), arrests witnessed by bystanders  
5 (AOR 4.13, 95% CI 3.35-5.09), good ADL before arrests (AOR 1.23, 95% CI  
6 1.03-1.47), VF as first documented rhythm (AOR 2.04, 95% CI 1.42-2.92), public  
7 places (AOR 1.45, 95% CI 1.10-1.91), intravenous fluid (AOR 1.45, 95% CI  
8 1.14-1.84), and early EMS response time (AOR for one-increment of minute 0.92, 95%  
9 CI 0.90-0.95) were associated with improving outcome. However, type of bystander  
10 CPR, intubation, and epinephrine were not associated with better outcome. Compared  
11 with asphyxia, the AORs were significantly lower in respiratory diseases (0.51, 95%  
12 CI 0.40-0.65), malignant tumors (0.06, 95% CI 0.03-0.11), stroke (0.27, 95% CI  
13 0.20-0.38), hanging (0.56, 95% CI 0.41-0.77), fall (0.03, 95% CI 0.01-0.06), drowning  
14 (0.16, 95% CI 0.09-0.29), and traffic injury (0.05, 95% CI 0.03-0.10). The proportion  
15 of one-month survival of the whole OHCAs with non-cardiac origin did not  
16 significantly increase (from 4.3% [86/2023] in 2005 to 4.9% [105/2126] in 2011) and  
17 the AOR for one-increment of year was 1.01 (95% CI 0.97-1.06). The AORs of  
18 neurologically favorable outcome after OHCAs with non-cardiac origin were almost

1 similar to those of one-month survival.

2 Subgroup analyses after dividing the two groups (internal and external causes) are  
3 shown in Supplemental Table. As for internal causes, arrests witnessed by bystanders  
4 (AOR 2.86, 95% CI 1.99-4.11), VF as first documented rhythm (AOR 2.35, 95% CI  
5 1.30-4.24), and public places (AOR 2.01, 95% CI 1.21-3.36) were associated with  
6 improving outcome. As for external causes, adults (AOR 1.51, 95% CI 1.17-1.96),  
7 arrests witnessed by bystanders (AOR 5.03, 95% CI 3.71-6.81), good ADL before  
8 arrests (AOR 1.34, 95% CI 1.08-1.67), intravenous fluid (AOR 1.69, 95% CI  
9 1.27-2.25), and early EMS response time (AOR for one-increment of minute 0.93, 95%  
10 CI 0.90-0.96) were associated with improving outcome.

11

1  
2  
3  
4  
5  
6 **1 DISCUSSION**  
7

8  
9 2 The extensive OHCA registry in Osaka showed that one-month survival after OHCA  
10  
11 3 with non-cardiac origin was poor and the survival trends did not improve year-by-year.

12  
13  
14 4 In addition, the survivals differed by detailed non-cardiac origin. To further improve  
15  
16 5 survival after OHCA, sufficient attention should be paid to the epidemiological  
17  
18 6 characteristics of OHCA with non-cardiac origin as much as those of OHCA with  
19  
20 7 cardiac origin, and this study describing the actual situation regarding the incidence  
21  
22 8 and outcome of OHCA with non-cardiac origin provides valuable information to  
23  
24 9 improve the survival.  
25  
26  
27  
28  
29  
30  
31

32 10 Our study observed that the outcomes of OHCA with non-cardiac origin were poor  
33  
34 11 and stable during the seven years. In a previous study in Japan, neurologically  
35  
36 12 favorable outcome of bystander-witnessed OHCA with non-cardiac origin increased  
37  
38 13 from 2005 to 2011, but the absolute survival was very low,<sup>7</sup> and this result was similar  
39  
40 14 with ours. Improving the outcome of OHCA with non-cardiac origin poses an  
41  
42 15 important problem in resuscitation science because 20~40% of adult OHCA are of  
43  
44 16 non-cardiac origin.<sup>7-13</sup> In addition, the survivals exceedingly differed by detailed  
45  
46 17 non-cardiac origin, which also suggests the need and importance of an origin-specific  
47  
48 18 strategy for improving the outcomes.  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 We also showed that the OHCA incidence trends differed by detailed non-cardiac  
2 origin. For instance, the incidence rate of OHCA due to strokes significantly  
3 decreased during the study period. Although the reasons for the decrement were  
4 unclear, better blood pressure control and decreasing smoking rate in recent years of  
5 Japan might be one of the possible explanations for this phenomenon.<sup>20</sup> In fact, the  
6 numbers of stroke patients in Japan has also been decreasing.<sup>21</sup> On the other hand, the  
7 incidence rates of OHCA with external causes in our region increased and the  
8 outcomes after OHCA with external causes excluding asphyxia were miserable.  
9 However, there were regional variations on the incidence and outcome from OHCA  
10 with external causes.<sup>22,23</sup> For example, external OHCA due to trauma, drug overdose,  
11 or hanging in metropolitan area of Australia were more common and the survivals from  
12 traumatic and hanging-associated OHCA were not always futile, and the  
13 countermeasures would, therefore, differ by regions. Most importantly, more efforts  
14 should focus on prevention of OHCA with external causes because many of them are  
15 preventable.<sup>1-4</sup>

16 In a multivariable analysis, intravenous fluid administration was associated with  
17 better one-month survival after OHCA with non-cardiac origin. In preceding studies,  
18 prehospital intravenous fluid for OHCA including both cardiac and non-cardiac

1 origins was not associated with the improved outcome,<sup>24</sup> whereas intravenous access  
2 were associated with a reduction in hospital mortality among non-injured, non-cardiac  
3 arrest patients<sup>25</sup> Thus, the effects of fluid administration on prehospital emergency  
4 patients were under debate, and further investigations by other cohorts or randomized  
5 controlled trials are needed to confirm these associations.

6 In this study, a multivariate analysis also underscored that either bystander-initiated  
7 chest compression-only CPR or conventional CPR with rescue breathing was not  
8 effective for OHCA with non-cardiac origin. From a nationwide study focused on  
9 43,000 bystander-witnessed OHCA with non-cardiac origin, we demonstrated that  
10 conventional CPR with rescue breathing had an incremental benefit for OHCA with  
11 non-cardiac origin, but the impact on the overall survival after OHCA was small.<sup>8</sup>

12 Considering these results, the effectiveness of bystander CPR on OHCA with  
13 non-cardiac origin in our region might be related to the significantly high rates of  
14 attempted EMS resuscitation in Japan compared with western countries.<sup>22,26</sup> However,  
15 as recommended in the CPR guidelines,<sup>1-4</sup> bystander CPR plays a key role in the  
16 “chain of survival” and increasing the proportion of bystander CPR for OHCA patients  
17 is important.

18 Furthermore, factors such as arrests witnessed by bystanders and earlier EMS

1  
2  
3  
4  
5  
6 1 response time were also independent predictors of better outcome after OHCA with  
7  
8  
9 2 non-cardiac origin in a multivariate analysis. This would indicate the importance of an  
10  
11 3 early EMS activation in the chain of survival<sup>1-4</sup> and suggests that activating the EMS  
12  
13 4 system quickly leads to improving the outcomes after OHCA with non-cardiac origin.  
14  
15  
16  
17 5 In addition, the verification of the effects on prehospital emergency care as well as  
18  
19  
20 6 in-hospital treatment is essential to improve survival after OHCA with non-cardiac  
21  
22  
23 7 origin.  
24  
25

26 8 The present study has some inherent limitations. First, the category of presumed  
27  
28 9 cardiac or non-cardiac causes is made clinically, as per the Utstein-style international  
29  
30 10 guidelines for cardiac arrest data reporting.<sup>14,15</sup> Second, information on post-arrest care  
31  
32 11 is lacking. In-hospital treatment (e.g., hemodynamic support, cardiovascular  
33  
34 12 intervention, induced hypothermia) might affect survival after OHCA.<sup>27</sup> Third,  
35  
36 13 unmeasured confounding factors may have influenced the association between OHCA  
37  
38 14 with non-cardiac origin and the outcome.  
39  
40  
41  
42  
43  
44  
45

46  
47 15

## 48 49 16 **CONCLUSION**

50  
51  
52 17 The large OHCA registry in Osaka demonstrated that one-month survival after OHCA  
53  
54 18 with non-cardiac origin was poor, the survival trends did not improve year-by-year, and  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 the survivals differed by detailed non-cardiac origin. Further monitoring and discussion  
2 for epidemiology and outcome of OHCA with non-cardiac origin are warranted to  
3 improve survival after OHCA in this group.

4

For peer review only



1  
2  
3  
4  
5  
6 **1 Acknowledgments**  
7

8  
9 2 We are deeply indebted to all of the EMS personnel and concerned physicians in Osaka  
10  
11 3 Prefecture, and the Osaka Medical Association for their indispensable cooperation and  
12  
13 4 generous support. We also thank all members of the Utstein Osaka Project for their  
14  
15 5 contribution in the organization, coordination, and oversight as the steering committee.  
16  
17  
18  
19  
20  
21  
22

23 **7 Contributors**  
24

25  
26 8 All authors (TK, KK, TS, TI, CN, KK, TN, YH, YK, KY, and TS) participated in the study  
27  
28 9 conception and design, acquisition of data, analysis and interpretation of data, drafting the  
29  
30 10 article and revising it critically for important intellectual content, and final approval of the  
31  
32 11 manuscript.  
33  
34  
35  
36  
37  
38  
39  
40

41 **13 Funding**  
42

43  
44 14 This study was supported by a scientific research grant from the Ministry of Health, Labour,  
45  
46 15 and Welfare of Japan (25112601).  
47  
48  
49  
50

51  
52 **17 Competing interests**  
53

54  
55 18 None.  
56  
57  
58  
59  
60

1

**2 Ethics approval**

3 The study was approved by the institutional review board of Osaka University with the assent  
4 of the EMS authorities of the local governments in Osaka Prefecture.

5

**6 Provenance and peer review**

7 Not commissioned; externally peer reviewed.

8

**9 Data sharing statement**

10 TK had full access to all of the data in the study and takes responsibility for the integrity of the  
11 data and the accuracy of the data analysis.

12

**13 Open Access**

14 This is an Open Access article distributed in accordance with the Creative Commons  
15 Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute,  
16 remix, adapt, build upon this work noncommercially, and license their derivative works on  
17 different terms, provided the original work is properly cited and the use is non-commercial.

18 See: <http://creativecommons.org/licenses/by-nc/3.0/>

19

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## 1 REFERENCES

- 2 1. 2010 International consensus on cardiopulmonary resuscitation and emergency  
3 cardiovascular care science with treatment recommendations. *Circulation*  
4 2010;122:S250-605.
- 5 2. 2010 American Heart Association guidelines for cardiopulmonary resuscitation and  
6 emergency cardiovascular care. *Circulation* 2010;122:S639-946.
- 7 3. European Resuscitation Council Guidelines for Resuscitation 2010. *Resuscitation*  
8 2010;81:1219-451.
- 9 4. 2010 Japanese guidelines for emergency care and cardiopulmonary resuscitation. 1st ed.  
10 Tokyo: Health Shuppansha; 2011 (in Japanese).
- 11 5. Iwami T, Nichol G, Hiraide A, *et al.* Continuous improvements of chain of survival  
12 increased survival after out-of-hospital cardiac arrests: a large-scale population-based  
13 study. *Circulation* 2009;119:728-34.
- 14 6. Rea TD, Helbock M, Perry S, *et al.* Increasing use of cardiopulmonary resuscitation  
15 during out-of-hospital ventricular fibrillation arrest: survival implications of guideline  
16 changes. *Circulation* 2006;114:2760-5.
- 17 7. Kitamura T, Iwami T, Kawamura T, *et al.* Nationwide improvements in survival from  
18 out-of-hospital cardiac arrests in Japan. *Circulation* 2012;126:2834-43.

- 1  
2  
3  
4  
5  
6 1 8. Kitamura T, Iwami T, Kawamura T, *et al.* Bystander-initiated rescue breathing for  
7  
8  
9 2 out-of-hospital cardiac arrests of non-cardiac origin. *Circulation* 2010;122:293-9.  
10  
11  
12 3 9. Kuisma M, Alaspää A. Out-of-hospital cardiac arrests of non-cardiac origin.  
13  
14 4 Epidemiology and outcome. *Eur Heart J* 1997;18:1122-8.  
15  
16  
17 5 10. Engdahl J, Bång A, Karlson BW, *et al.* Characteristics and outcome among patients  
18  
19 6 suffering from out of hospital cardiac arrest of non-cardiac aetiology. *Resuscitation*  
20  
21 7 2003;57:33-41.  
22  
23  
24  
25  
26 8 11. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital  
27  
28 9 cardiac arrest of non-cardiac origin. *Resuscitation* 2007;72:200-7.  
29  
30  
31  
32 10 12. Iwami T, Hiraide A, Nakanishi N, *et al.* Age and sex analyses of out-of-hospital cardiac  
33  
34 11 arrest in Osaka, Japan. *Resuscitation* 2003;57:145-52.  
35  
36  
37  
38 12 13. Engdahl J, Holmberg M, Karlson BW, *et al.* The epidemiology of out-of-hospital 'sudden'  
39  
40 13 cardiac arrest. *Resuscitation* 2002;52:235-45.  
41  
42  
43  
44 14 14. Cummins RO, Chamberlain DA, Abramson NS, *et al.* Recommended guideline for  
45  
46 15 uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style: a statement  
47  
48 16 for health professionals from a task force of the American Heart Association, the  
49  
50 17 European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the  
51  
52 18 Australian Resuscitation Council. *Circulation* 1991;84:960-75.  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 15. Jacobs I, Nadkarni V, Bahr J, *et al.* Cardiac arrest and cardiopulmonary resuscitation  
7  
8  
9 2 outcome reports: update and simplification of the Utstein templates for resuscitation  
10  
11 3 registries: a statement for healthcare professionals from a task force of the International  
12  
13 4 Liaison Committee on Resuscitation (American Heart Association, European  
14  
15 Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation  
16  
17 5 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
18  
19 6 Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation,  
20  
21 7 Resuscitation Councils of Southern Africa). *Circulation* 2004;110:3385-97.  
22  
23  
24  
25  
26 8 16. Nitta M, Iwami T, Kitamura T, *et al.* Age-specific differences in outcomes after  
27  
28 9 out-of-hospital cardiac arrests. *Pediatrics* 2011;128:e812-20.  
29  
30  
31  
32 10 17. Atkins DL, Everson-Stewart S, Sears GK, *et al.* Epidemiology and outcomes from  
33  
34 11 out-of-hospital cardiac arrest in children: the Resuscitation Outcomes Consortium  
35  
36 12 Epistry-Cardiac Arrest. *Circulation* 2009;119:1484-91.  
37  
38  
39  
40  
41 13 18. 2010 Population Census of Japan.  
42  
43 14 [http://www.stat.go.jp/data/kokusei/2010/index.htm?utm\\_source=twitterfeed&utm\\_mediu](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter)  
44  
45 15 [m=twitter](http://www.stat.go.jp/data/kokusei/2010/index.htm?utm_source=twitterfeed&utm_medium=twitter) (Accessed August 05, 2014) (in Japanese).  
46  
47  
48  
49 16 19. Vital Statistics of Japan 2005. Tokyo: Health and Welfare Statistics Association; 2007.  
50  
51  
52  
53 17 20. Hata J, Ninomiya T, Hirakawa Y, *et al.* Secular trends in cardiovascular disease and its  
54  
55 18 risk factors in Japanese: half-century data from the Hisayama Study (1961-2009).  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6 1 *Circulation* 2013;128:1198-205.  
7  
8  
9 2 21. 2011 Overview of Patient Survey. <http://www.mhlw.go.jp/toukei/saikin/hw/kanja/11/>  
10  
11  
12 3 (Accessed August 05, 2014) (in Japanese).  
13  
14 4 22. Deasy C, Bray J, Smith K, *et al.* Traumatic out-of-hospital cardiac arrests in Melbourne,  
15  
16  
17 5 Australia. *Resuscitation* 2012;83:465-70.  
18  
19  
20 6 23. Deasy C, Bray J, Smith K, *et al.* Hanging-associated out-of-hospital cardiac arrests in  
21  
22  
23 7 Melbourne, Australia. *Emerg Med J* 2013;30:38-42.  
24  
25  
26 8 24. Hagihara A, Hasegawa M, Abe T, *et al.* Prehospital lactated ringer's solution treatment  
27  
28  
29 9 and survival in out-of-hospital cardiac arrest: a prospective cohort analysis. *PLoS Med*  
30  
31  
32 10 2013;10:e1001394.  
33  
34  
35 11 25. Seymour CW, Cooke CR, Hebert PL, *et al.* Intravenous access during out-of-hospital  
36  
37  
38 12 emergency care of noninjured patients: a population-based outcome study. *Ann Emerg*  
39  
40  
41 13 *Med* 2012;59:296-303.  
42  
43  
44 14 26. Nichol G, Thomas E, Callaway CW, *et al.* Regional variation in out-of-hospital cardiac  
45  
46  
47 15 arrest incidence and outcome. *JAMA* 2008;300:1423-31.  
48  
49  
50 16 27. Neumar RW, Nolan JP, Adrie C, *et al.* Post-cardiac arrest syndrome: epidemiology,  
51  
52  
53 17 pathophysiology, treatment, and prognostication. A Scientific Statement from the  
54  
55  
56 18 International Liaison Committee on Resuscitation; the American Heart Association  
57  
58  
59  
60

1  
2  
3  
4  
5  
6 1 Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and  
7  
8  
9 2 Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the  
10  
11  
12 3 Council on Clinical Cardiology; the Council on Stroke. *Circulation* 2008;118:2452-8.  
13  
14  
15 4

For peer review only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 **Figure Legends**

2 **Figure 1** Overview of EMS-treated cardiac arrests with an abridged Utstein template from  
3 January 1, 2005 to December 31, 2011. EMS, emergency medical service.

For peer review only



**Table 1** Age-adjusted incidences and unadjusted one-month survival rate of out-of-hospital cardiac arrests with non-cardiac origin according to the cause over time

	2005	2006	2007	2008	2009	2010	2011	P for trend
Age-adjusted Incidence per 100,000 persons								
External causes	12.4	12.3	13.2	12.8	13.2	13.3	13.3	0.024
Asphyxia	2.7	3.0	2.8	3.4	3.1	2.9	2.9	0.726
Hanging	3.4	3.4	4.1	3.4	3.7	3.9	3.9	0.158
Fall	2.4	2.5	3.1	2.4	2.9	3.0	2.7	0.396
Drowning	1.2	1.1	1.2	1.4	1.2	1.3	1.6	0.065
Traffic injury	1.6	1.5	1.4	1.4	1.4	1.5	1.4	0.229
Drug overdose	0.5	0.4	0.2	0.4	0.4	0.4	0.3	0.304
Unclassified	0.5	0.5	0.4	0.3	0.5	0.4	0.5	0.447
Respiratory diseases	2.2	1.8	1.8	1.7	1.3	1.3	1.6	0.018
Malignant tumors	1.6	1.8	1.8	1.7	1.5	1.3	1.6	0.109
Strokes	2.0	1.8	1.8	1.6	1.4	1.2	1.3	< 0.001
Others	2.7	3.3	3.1	2.9	2.7	2.5	2.4	0.087
Unadjusted one-month survival, % (n/N)								
External causes	4.8 (53/1100)	6.8 (72/1059)	5.7 (66/1164)	7.2 (85/1184)	7.1 (86/1207)	6.1 (75/1225)	5.6 (73/1300)	0.736
Asphyxia	10.4 (35/337)	15.4 (53/344)	13.0 (44/338)	15.6 (67/430)	16.3 (66/406)	14.8 (58/393)	14.0 (59/422)	0.374
Hanging	4.6 (12/261)	4.7 (12/255)	5 (16/318)	4.8 (13/273)	4.9 (14/287)	3.3 (10/301)	2.3 (7/304)	0.101
Fall	0.6 (1/159)	0.6 (1/169)	0.9 (2/219)	1.2 (2/165)	0.0 (0/197)	0.5 (1/208)	1.1 (2/183)	NA
Drowning	1.3 (2/151)	3.3 (4/120)	0.0 (0/128)	1.3 (2/159)	2.1 (3/144)	0.7 (1/148)	0.0 (0/212)	NA
Traffic injury	0.9 (1/116)	1.0 (1/101)	1.8 (2/109)	0.9 (1/106)	1.9 (2/103)	1.7 (2/115)	2.6 (3/115)	0.027

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

Drug overdose	3.0 (1/33)	0.0 (0/29)	5.6 (1/18)	0.0 (0/25)	3.3 (1/30)	11.1 (3/27)	4.0 (1/25)	NA
Unclassified	2.3 (1/43)	2.4 (1/41)	2.9 (1/34)	0.0 (0/26)	0.0 (0/40)	0.0 (0/33)	2.6 (1/39)	NA
Respiratory diseases	6.4 (17/267)	3.9 (8/206)	8.0 (17/212)	9.8 (21/214)	6.7 (11/165)	4.7 (8/169)	5.6 (12/215)	0.875
Malignant tumors	0.5 (1/186)	0.5 (1/194)	1.0 (2/202)	1.0 (2/196)	0.0 (0/178)	2.5 (4/159)	0.5 (1/194)	NA
Strokes	3.6 (7/196)	6.1 (11/179)	4.5 (8/176)	3.2 (5/154)	4.9 (7/143)	6.0 (8/134)	6.8 (9/132)	0.241
Others	2.9 (8/277)	7.0 (22/314)	1.3 (4/308)	4.5 (14/311)	4.3 (12/278)	5.3 (15/281)	3.5 (10/285)	0.808

NA indicates not analyzed.

For peer review only

**Table 2** Patient and EMS characteristics of out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n=14,164)	External causes (n = 8239)	Respiratory diseases (n=1448)	Malignant tumors (n=1309)	Strokes (n=1114)	Others (n=2054)	<i>P</i> value*
Age, yr, mean (SD)	66.8 (19.0)	63.5 (20.5)	76.1 (14.2)	71.9 (12.0)	67.7 (14.7)	69.8 (17.6)	< 0.001
Age group, n (%)							< 0.001
Adults aged 20-64 years	5513 (38.9)	3826 (46.4)	229 (15.8)	345 (26.4)	447 (40.1)	666 (32.4)	
Elderly aged >=65 years	8651 (61.1)	4413 (53.6)	1219 (84.2)	964 (73.6)	667 (59.9)	1388 (67.6)	
Men, n (%)	8215 (58.0)	4789 (58.1)	844 (58.3)	881 (67.3)	559 (50.2)	1142 (55.6)	< 0.001
Arrests witnessed by bystanders, n (%)	5561 (39.3)	2952 (35.8)	682 (47.1)	639 (48.8)	493 (44.3)	795 (38.7)	< 0.001
Good activities of daily living, n (%)	8522 (60.2)	5213 (63.3)	653 (45.1)	443 (33.8)	896 (80.4)	1317 (64.1)	< 0.001
First documented rhythm, n (%)							< 0.001
VF	324 (2.3)	119 (1.4)	35 (2.4)	26 (2.0)	69 (6.2)	75 (3.7)	
PEA	3356 (23.7)	1853 (22.5)	394 (27.2)	262 (20.0)	329 (29.5)	518 (25.2)	
Asystole	10196 (72.0)	6124 (74.3)	983 (67.9)	1008 (77.0)	647 (58.1)	1434 (69.8)	
Others	288 (2.0)	143 (1.7)	36 (2.5)	13 (1.0)	69 (6.2)	27 (1.3)	
Location of arrest, n (%)							< 0.001
Homes	9010 (63.6)	4435 (53.8)	1098 (75.8)	1217 (93.0)	801 (71.9)	1459 (71.0)	
Public places	2035 (14.4)	1608 (19.5)	59 (4.1)	24 (1.8)	156 (14.0)	188 (9.2)	
Work places	346 (2.4)	223 (2.7)	7 (0.5)	4 (0.3)	48 (4.3)	64 (3.1)	
Health care facilities	1505 (10.6)	904 (11.0)	248 (17.1)	55 (4.2)	63 (5.7)	235 (11.4)	
Others	1268 (9.0)	1069 (13.0)	36 (2.5)	9 (0.7)	46 (4.1)	108 (5.3)	
Public-access AED use, n (%)	13 (0.1)	4 (0.05)	2 (0.1)	0 (0.0)	5 (0.4)	2 (0.1)	0.001
Type of Bystander CPR, n (%)							< 0.001
No CPR	9023 (63.7)	5383 (65.3)	836 (57.7)	889 (67.9)	633 (56.8)	1282 (62.4)	
Chest compression-only CPR	3288 (23.2)	1811 (22.0)	408 (28.2)	297 (22.7)	283 (25.4)	489 (23.8)	

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

Conventional CPR with rescue breathing	1853 (13.1)	1045 (12.7)	204 (14.1)	123 (9.4)	198 (17.8)	283 (13.8)	
Intravascular fluid, n (%)	2320 (16.4)	1458 (17.7)	202 (14.0)	113 (8.6)	230 (20.6)	317 (15.4)	< 0.001
Intubation, n (%)	2639 (18.6)	1364 (16.6)	338 (23.3)	242 (18.5)	257 (23.1)	438 (21.3)	< 0.001
Epinephrine, n (%)	987 (7.0)	572 (6.9)	88 (6.1)	49 (3.7)	125 (11.2)	153 (7.4)	< 0.001
Call to contact with a patient by EMS (EMS response time), min, mean (SD)	7.9 (4.1)	8.0 (4.6)	7.7 (3.0)	7.7 (2.7)	7.7 (2.8)	7.9 (3.8)	0.003
Call to CPR by EMS, min, mean (SD)	8.5 (4.5)	8.8 (5.1)	8.1 (3.1)	8.1 (2.8)	8.2 (2.9)	8.4 (4.2)	< 0.001
Call to hospital arrival, min, mean (SD)	28.2 (8.6)	28.4 (8.6)	27.3 (8.2)	28.0 (8.9)	28.2 (8.4)	28.1 (8.7)	0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

Data on the times from call to contact with a patient, CPR by EMS, and hospital arrival were missing for 33, 40, and 166 victims, respectively.

**Table 3** Patient and EMS characteristics of out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Age, yr, mean (SD)	77.9 (14.4)	55.6 (17.4)	47.4 (17.4)	73.1 (14.8)	52.6 (19.0)	49.9 (19.5)	58.1 (19.3)	< 0.001
Age group, n (%)								< 0.001
Adults aged 20-64 years	403 (15.1)	1136 (66.8)	1055 (81.2)	210 (19.8)	523 (68.4)	141 (75.4)	158 (61.7)	
Elderly aged ≥65 years	2267 (84.9)	663 (33.2)	245 (18.8)	852 (80.2)	242 (31.6)	46 (24.6)	98 (38.3)	
Men, n (%)	1345 (50.4)	1290 (64.5)	781 (60.1)	530 (49.9)	558 (72.9)	117 (62.6)	168 (65.6)	< 0.001
Arrests witnessed by bystanders, n (%)	1801 (67.5)	27 (1.4)	510 (39.2)	56 (5.3)	476 (62.2)	10 (5.3)	72 (28.1)	< 0.001
Good activities of daily living, n (%)	1099 (41.2)	1769 (88.5)	685 (52.7)	854 (80.4)	517 (67.6)	133 (71.1)	156 (60.9)	< 0.001
First documented rhythm, n (%)								< 0.001
VF	56 (2.1)	13 (0.7)	19 (1.5)	12 (1.1)	14 (1.8)	1 (0.5)	4 (1.6)	
PEA	960 (36.0)	198 (9.9)	274 (21.1)	72 (6.8)	259 (33.9)	20 (10.7)	70 (27.3)	
Asystole	1589 (59.5)	1775 (88.8)	985 (75.8)	970 (91.3)	469 (61.3)	160 (85.6)	176 (68.8)	
Others	65 (2.4)	13 (0.7)	22 (1.7)	8 (0.8)	23 (3.0)	6 (3.2)	6 (2.3)	
Location of arrest, n (%)								< 0.001
Homes	1596 (59.8)	1667 (83.4)	139 (10.7)	770 (72.5)	2 (0.3)	150 (80.2)	111 (43.4)	
Public places	139 (5.2)	86 (4.3)	553 (42.5)	83 (7.8)	677 (88.5)	14 (7.5)	56 (21.9)	
Workplaces	35 (1.3)	94 (4.7)	44 (3.4)	3 (0.3)	7 (0.9)	7 (3.7)	33 (12.9)	
Health care facilities	835 (31.3)	27 (1.4)	12 (0.9)	14 (1.3)	1 (0.1)	0 (0.0)	15 (5.9)	
Others	65 (2.4)	125 (6.3)	552 (42.5)	192 (18.1)	78 (10.2)	16 (8.6)	41 (16.0)	

1										
2										
3										
4										
5										
6										
7	Public-access AED use, n (%)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.214
8	Type of Bystander CPR, n (%)									< 0.001
9	No CPR	1386 (51.9)	1174 (58.7)	1191 (91.6)	608 (57.3)	673 (88.0)	154 (82.4)	197 (77.0)		
10	Chest compression-only CPR	748 (28.0)	549 (27.5)	93 (7.2)	281 (26.5)	74 (9.7)	23 (12.3)	43 (16.8)		
11	Conventional CPR with rescue									
12	breathing	536 (20.1)	276 (13.8)	16 (1.2)	173 (16.3)	18 (2.4)	10 (5.3)	16 (6.2)		
13	Intravascular fluid, n (%)	540 (20.2)	393 (19.7)	107 (8.2)	281 (26.5)	76 (9.9)	27 (14.4)	34 (13.3)		< 0.001
14	Intubation, n (%)	800 (30.0)	167 (8.4)	41 (3.2)	251 (23.6)	31 (4.1)	33 (17.6)	41 (16.0)		< 0.001
15	Epinephrine, n (%)	326 (12.2)	83 (4.2)	41 (3.2)	68 (6.4)	37 (4.8)	6 (3.2)	11 (4.3)		< 0.001
16	Call to contact with a patient by EMS (EMS									
17	response time), min, mean (SD)	7.6 (2.9)	7.8 (3.3)	7.4 (3.3)	9.4 (7.6)	7.6 (4.2)	14.2 (10.7)	9.4 (7.3)		< 0.001
18	Call to CPR by EMS personnel, min, mean									
19	(SD)	7.9 (3.1)	8.6 (3.9)	8.2 (3.8)	10.0 (7.5)	9.3 (5.9)	14.4 (10.0)	11.0 (8.7)		< 0.001
20	Call to hospital arrival, min, mean (SD)	28.6 (8.6)	28.2 (7.9)	27.5 (8.3)	29.1 (9.3)	27.1 (8.8)	32.1 (11.1)	29.5 (9.4)		< 0.001

\*P values are calculated to test the homogeneity among the 7 cause groups.

EMS indicates emergency medical services; CPR, cardiopulmonary resuscitation; VF, ventricular fibrillation; PEA, pulseless electrical activity; AED, automated external defibrillator; SD, standard deviation.

**Table 4** Outcomes after out-of-hospital cardiac arrests with non-cardiac origin according to the cause

	Total (n = 1,4164)	External causes (n = 8239)	Respiratory diseases (n = 1448)	Malignant tumors (n = 1309)	Strokes (n = 1114)	Others (n =2054)	<i>P</i> value *
Prehospital ROSC, n (%)	1229 (8.7)	703 (8.5)	114 (7.9)	57 (4.4)	216 (19.4)	139 (6.8)	< 0.001
Total ROSC, n (%)	4744 (33.5)	2638 (32.0)	620 (42.8)	234 (17.9)	650 (58.3)	602 (29.3)	< 0.001
Hospital admission, n (%)	4142 (29.2)	2356 (28.6)	530 (36.6)	173 (13.2)	585 (52.5)	498 (24.2)	< 0.001
One-month survival, n (%)	755 (5.3)	510 (6.2)	94 (6.5)	11 (0.8)	55 (4.9)	85 (4.1)	< 0.001
Neurologically favorable outcome, n (%)	188 (1.3)	105 (1.3)	27 (1.9)	2 (0.2)	17 (1.5)	37 (1.8)	< 0.001

\*P values are calculated to test the homogeneity among the 5 cause groups.

ROSC indicates return of spontaneous circulation.

Data on one-month survival and neurological status were missing for 7 victims.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49

**Table 5** Outcomes after out-of-hospital cardiac arrests with external causes according to the cause

	Asphyxia (n = 2670)	Hanging (n = 1999)	Fall (n = 1300)	Drowning (n = 1062)	Traffic injury (n = 765)	Drug overdose (n = 187)	Unclassified (n = 256)	<i>P</i> value*
Prehospital ROSC, n (%)	463 (17.3)	144 (7.2)	22 (1.7)	36 (3.4)	28 (3.7)	4 (2.1)	6 (2.3)	< 0.001
Total ROSC, n (%)	1003 (37.6)	1500 (75.0)	1213 (93.3)	894 (84.2)	637 (83.3)	143 (76.5)	211 (82.4)	< 0.001
Hospital admission, n (%)	1529 (57.3)	453 (22.7)	62 (4.8)	147 (13.8)	92 (12.0)	40 (21.4)	33 (12.9)	< 0.001
One-month survival, n (%)	382 (14.3)	84 (4.2)	9 (0.7)	12 (1.1)	12 (1.6)	7 (3.7)	4 (1.6)	< 0.001
Neurologically favorable outcome, n (%)	71 (2.7)	17 (0.9)	1 (0.1)	4 (0.4)	6 (0.8)	4 (2.1)	2 (0.8)	< 0.001

\*P values are calculated to test the homogeneity among the 7 cause groups.

ROSC indicates return of spontaneous circulation.



**Table 6** Factors associated with outcomes after out-of-Hospital cardiac arrests with non-cardiac origin

	One-month survival				Neurologically favorable outcome			
	Crude OR	(95% CI)	Adjusted OR	(95% CI)	Crude OR	(95% CI)	Adjusted OR	(95% CI)
Adults (versus elderly)	0.95	(0.82-1.10)	1.36	(1.12-1.65)	1.02	(0.76-1.37)	1.52	(1.07-2.15)
Men	0.75	(0.64-0.88)	0.99	(0.84-1.16)	1.09	(0.81-1.46)	0.91	(0.67-1.24)
Witnessed by bystanders	4.41	(3.74-5.19)	4.13	(3.35-5.09)	4.48	(3.23-6.21)	4.83	(3.21-7.29)
Good activities of daily living	0.93	(0.80-1.08)	1.23	(1.03-1.47)	1.39	(1.02-1.88)	1.43	(1.02-2.02)
VF	2.74	(1.96-3.82)	2.04	(1.42-2.92)	7.72	(5.05-11.79)	5.40	(3.40-8.59)
Type of bystander CPR								
No CPR	Reference		Reference		Reference		Reference	
Chest compression-only CPR	0.97	(0.81-1.16)	0.80	(0.66-0.98)	0.95	(0.67-1.35)	0.92	(0.64-1.33)
Conventional CPR with rescue breathing	1.47	(1.20-1.79)	1.07	(0.86-1.34)	1.01	(0.65-1.55)	0.89	(0.56-1.42)
Type of non-cardiac origin								
Respiratory diseases	0.42	(0.33-0.53)	0.51	(0.40-0.65)	0.70	(0.44-1.09)	0.76	(0.48-1.21)
Malignant tumors	0.05	(0.03-0.09)	0.06	(0.03-0.11)	0.06	(0.01-0.23)	0.06	(0.01-0.23)
Strokes	0.31	(0.23-0.42)	0.27	(0.20-0.38)	0.57	(0.33-0.97)	0.34	(0.19-0.61)
Asphyxia	Reference		Reference		Reference		Reference	
Hanging	0.26	(0.21-0.34)	0.56	(0.41-0.77)	0.31	(0.18-0.53)	0.55	(0.28-1.07)
Fall	0.04	(0.02-0.08)	0.03	(0.01-0.06)	0.03	(0.004-0.20)	0.01	(0.002-0.11)
Drowning	0.07	(0.04-0.12)	0.16	(0.09-0.29)	0.14	(0.05-0.38)	0.31	(0.11-0.90)

1							
2							
3							
4							
5							
6							
7	Traffic injury	0.10 (0.05-0.17)	0.05 (0.03-0.10)	0.29 (0.13-0.67)	0.10 (0.04-0.26)		
8							
9	Drug overdose	0.23 (0.11-0.50)	0.58 (0.26-1.29)	0.80 (0.29-2.21)	1.74 (0.58-5.19)		
10							
11	Others	0.26 (0.20-0.33)	0.29 (0.22-0.38)	0.67 (0.45-1.00)	0.60 (0.39-0.92)		
12							
13	Unclassified	0.10 (0.04-0.26)	0.10 (0.04-0.28)	0.29 (0.07-1.18)	0.27 (0.06-1.16)		
14							
15	Location of arrest						
16							
17	Homes	Reference	Reference	Reference	Reference		
18							
19	Public places	0.78 (0.61-0.99)	1.45 (1.10-1.91)	1.11 (0.75-1.65)	1.54 (0.97-2.44)		
20							
21	Workplaces	1.29 (0.83-1.98)	1.40 (0.87-2.23)	1.26 (0.55-2.89)	0.95 (0.39-2.30)		
22							
23	Health care facilities	1.69 (1.38-2.07)	0.88 (0.69-1.12)	0.72 (0.42-1.24)	0.47 (0.26-0.85)		
24							
25	Others	0.70 (0.51-0.94)	1.67 (1.19-2.35)	0.68 (0.38-1.24)	1.35 (0.72-2.54)		
26							
27	Intravascular fluid	1.78 (1.50-2.11)	1.45 (1.14-1.84)	1.34 (0.94-1.91)	1.52 (0.97-2.38)		
28							
29	Intubation	1.62 (1.37-1.92)	1.02 (0.84-1.23)	0.73 (0.48-1.10)	0.50 (0.32-0.77)		
30							
31	Epinephrine	2.32 (1.87-2.88)	0.97 (0.71-1.32)	1.25 (0.74-2.09)	0.60 (0.31-1.17)		
32							
33	EMS response time (for one-increment of minute)	0.93 (0.91-0.96)	0.92 (0.90-0.95)	0.91 (0.86-0.96)	0.90 (0.84-0.95)		
34							
35	Year (for one-increment of year)	1.02 (0.98-1.06)	1.01 (0.97-1.06)	1.02 (0.95-1.09)	1.05 (0.97-1.13)		

VF denotes ventricular fibrillation; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OR, odds ratio; CI, confidence interval.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

1	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and
2			sensitivity analyses
3			
4	<b>Discussion</b>		
5	Key results	18	Summarise key results with reference to study objectives
6			
7	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
8			imprecision. Discuss both direction and magnitude of any potential bias
9			
10	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
11			multiplicity of analyses, results from similar studies, and other relevant evidence
12	Generalisability	21	Discuss the generalisability (external validity) of the study results
13			
14	<b>Other information</b>		
15	Funding	22	Give the source of funding and the role of the funders for the present study and, if
16			applicable, for the original study on which the present article is based
17			

18  
19 \*Give information separately for exposed and unexposed groups.

20  
21 **Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and  
22 published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely  
23 available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at  
24 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is  
25 available at <http://www.strobe-statement.org>.  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60