Journal of the American Heart Association

ORIGINAL RESEARCH

Underlying Cause of Out-of-Hospital Cardiac Arrests in Japan in Survivors Versus Nonsurvivors

Satoshi Yoshimura, MD, MPH; Zian H. Tseng, MD, MAS; Tomoki Yamada, MD, PhD; Shunichiro Nakao, MD, PhD; Kazuhisa Yoshiya, MD, PhD; Changhwi Park, MD; Tetsuro Nishimura, MD, PhD; Takuya Ishibe, MD, PhD; Kazuma Yamakawa, MD, PhD; Takeyuki Kiguchi, MD, PhD; Masafumi Kishimoto, MD, PhD; Kohei Ninomiya, MD; Yusuke Ito, MD; Taku Sogabe, MD, PhD; Takaya Morooka, MD, PhD; Haruko Sakamoto, MD; Yuki Hironaka, MD; Atsunori Onoe, MD; Tasuku Matsuyama, MD, PhD; Yohei Okada, MD, PhD; Satoshi Matsui, MD, PhD; Norihiro Nishioka, MD, PhD; Shunsuke Kimata, MD, MPH; Shunsuke Kawai, MD, MPH; Yuto Makino, MD, PhD; Ling Zha, PhD; Kosuke Kiyohara, DPH; Tetsuhisa Kitamura, MD, MSc, DPH; Taku Iwami, MD, MPH, PhD; on behalf of the CRITICAL Study Group Investigators

BACKGROUND: The causes underlying out-of-hospital cardiac arrest (OHCA) are rarely investigated. This study aimed to investigate causes of OHCA in CRITICAL (Comprehensive Registry of In-Hospital Intensive Care for OHCA Survival), a multicenter OHCA registry in Osaka, Japan.

METHODS: Nontraumatic patients with OHCA (by CARES [Cardiac Arrest Registry to Enhance Survival] criteria) aged 18 to 90 years between July 1, 2012 and December 31, 2020 were included. By Japanese law, all patients with OHCA (resuscitated or not) must be transported to the emergency department where death is declared if resuscitation is unsuccessful; this latter group was considered presumed sudden cardiac deaths whereas those surviving to hospitalization were considered resuscitated OHCA. We compared underlying causes of OHCA in presumed sudden cardiac deaths, survivors of OHCA (alive 30 days after the event), and nonsurvivors of OHCA (died during hospitalization). Causes were confirmed when autopsy or postresuscitation hospital workup was performed and probable when determined by attending physician impression (partial workup).

RESULTS: Of 12 252 total OHCAs, 8005 (65.3%) were. presumed sudden cardiac deaths, 4247 (34.7%) were resuscitated, and 1293 (10.6%) were survivors. Resuscitated OHCA cardiac causes comprised 73.2% (n=3110) and noncardiac causes 26.8% (n=1137). Cardiac cause, most commonly acute coronary syndrome, was more prevalent in survivors of OHCA than nonsurvivors (85.7% [n=1137] versus 67.8% [n=2002]; $P<0.001$). Although 40.4% of the survived at 30 days cases were acute coronary syndrome, cerebrovascular disease accounted for 9.8% of nonsurvivors of OHCA and nearly one fifth (n=144, 17.8%) of middle-aged cases.

CONCLUSIONS: Cardiac cause was more common in survivors than cases dying in the emergency room (sudden deaths) or in hospital after initial resuscitation (nonsurvivors of OHCA). Causes in nonsurvivors of OHCA who died in hospital were more heterogeneous than those of survivors of OHCA, especially cerebrovascular emergencies.

Key Words: pathogenesis ■ out-of-hospital cardiac arrest ■ sudden cardiac arrest ■ sudden cardiac death

Correspondence to: Taku Iwami, MD, MPH, PhD, Department of Preventive Services, School of Public Health, Kyoto University 606-8501, YoshidaKonoecho, Sakyo, Kyoto, Japan. Email: iwami.taku.8w@kyoto-u.ac.jp

This article was sent to Thomas S. Metkus, MD, PhD, Associate Editor, for review by expert referees, editorial decision, and final disposition.

For Disclosures and Sources of Funding, see page 11.

JAHA is available at: www.ahajournals.org/journal/jaha

RESEARCH PERSPECTIVE

What Is New?

- This study reveals that nonsurvivors of out-of hospital cardiac arrest in Japan have more diverse underlying causes compared with survivors, with a higher proportion due to noncardiac causes such as cerebrovascular disease.

What Question Should Be Addressed Next?

- Future studies should focus more on the causes of out-of-hospital cardiac arrest with a clear definition and explore targeted preventive measures for nonarrhythmic out-of-hospital cardiac arrest.

Nonstandard Abbreviations and Acronyms

OHCA	out-of-hospital cardiac arrest
ROSC	return of spontaneous circulation
SCD	sudden cardiac death

Out-of-hospital cardiac arrest (OHCA) is a significant public health concern in the industrialized world, with approximately 120 000 events occurring in Japan and 360 000 in the United States annually.[1,2] The prognosis of OHCA has been improving but has remained low over the past decade.[3] Clarifying the underlying causes for cardiac arrest can facilitate cause-specific preventive strategies and therapies.

In recent studies of OHCA in San Francisco County, underlying arrhythmic causes accounted for 56% of those dying in the field (ie, sudden cardiac death [SCDs] that were confirmed cause by autopsy, in contrast to presumed SCDs in our study, which were not confirmed by autopsy)[4] and a nearly identical 57% of cases dying in the hospital after initial resuscitation, compared with 92% of survivors to hospital discharge,[5] suggesting that survivors of OHCA are not equivalent to SCDs or nonsurvivors of OHCA. Furthermore, these studies revealed that neurologic causes were highly lethal: none of the 1 in 5 resuscitated patients with OHCAs found to be due to neurologic causes survived. Thus, elucidating causes for OHCA, especially for nonsurvivors of OHCA, is critical to prevent and rescue this highest priority group and to ultimately reduce the high burden of presumed SCDs.

Therefore, in this study we sought to investigate underlying causes for OHCA in Japan and compare causes of cardiac arrest in presumed SCDs, and survivors and nonsurvivors after resuscitated OHCA in a large hospital-based registry in Osaka (population 8.8 million).

METHODS

The data are available from the authors upon reasonable request.

This study was conducted according to the Strengthening the Reporting of Observational Studies in Epidemiology Statement: guidelines for reporting observational studies[6] and was approved by the Ethics Committee of the Kyoto University Graduate School of Medicine (R1045) and each participating hospital. The requirement for individual patient consent was waived owing to the nature of the observational study.

Study Design and Setting

We analyzed the database from the CRITICAL (Comprehensive Registry of In-Hospital Intensive Care for OHCA Survival) study, which is a multicenter prospective observational data registry to collect both pre- and in-hospital data on OHCA treatment. A complete description of the study methodology has been reported previously.[7] Briefly, in Osaka Prefecture, Japan, all sequential patients with OHCA who underwent resuscitation attempts from July 1, 2012, onward were recorded. These patients were then transported to the institutions involved in this registry. The registry consists of 16 facilities: 15 critical care medical centers, each of which includes an emergency department, and 1 hospital that, although not a critical care medical center, is equipped with an emergency department. The Osaka Prefecture in Japan, the target area of the CRITICAL study, has an area of 1905 km^2 and a residential population of approximately 8.8 million inhabitants as of 2015.[8] In Osaka Prefecture, approximately 7500 OHCA cases occur annually.[9] From 2012 to 2020, approximately 2000 per year were included in the registry, accounting for approximately one fourth of total patients with OHCA.

Study Patients

We enrolled all patients aged ≥18 to 90 years who experienced OHCA, for whom resuscitation was attempted, and were transferred to the participating institutions between January 2012 and December 2020. We set the upper age limit because the causes of the older patients after OHCA tend not to evaluate well. OHCA was defined by emergency medical services (EMS) primary impression “cardiac arrest” as per CARES (Cardiac Arrest Registry to Enhance Survival) convention.[10] We excluded patients with OHCA who did not receive cardiopulmonary resuscitation by physicians after hospital arrival (ie, patients beyond resuscitative efforts). We also excluded patients with terminal cancer (ie, death not

unexpected) and OHCA caused by external causes, such as traffic trauma, falls, hanging, drowning, choking, drug use, and other identifiable external causes.[4,5] As per the Lancet Commission definition,[11] patients with OHCA were defined as presumed SCDs if they died in the emergency department or resuscitated OHCA if they were initially resuscitated and survived to hospital admission. This definition might lead to misunderstanding because the term SCD comprises subjects with noncardiac causes for OHCA and those with cardiac causes. However, the Lancet Commission proposed the use of the terminology "presumed SCD" for nonconfirmed case before autopsy, toxicology, and histology.[6] For this reason, we used the term "presumed SCDs" in this study. Resuscitated patients with OHCA were then further divided into 2 groups: survivors of OHCA who were alive 1 month after the event and nonsurvivors of OHCA who died in the hospital after initially surviving to admission. Because EMS in Japan cannot cease resuscitation at the scene or during transportation, nearly all patients with OHCA are transported to the emergency department where only an attending physician can pronounce death for patients beyond resuscitative efforts or who were not successfully resuscitated. Thus, nearly all out-of-hospital sudden deaths (ie, patients OHCA who are deceased at the scene or unsuccessfully resuscitated) in Japan are captured by final disposition in the emergency department. Therefore, although previous studies such as POST SCD (Postmortem Systematic Investigation of Sudden Cardiac Death) systematically included sudden death occurring out of hospital,[4,5] the presumed SCDs in this study did not include death out of the hospital or at the scene.

Emergency Medical Services in Japan

Previous publications from the CRITICAL study detail Japan's EMS system.[7] Briefly, the "119" emergency telephone number is accessible anywhere in Japan. After receiving a 119 call, the emergency dispatch center sends the nearest available ambulance to the site. Emergency services are provided 24 hours a day and 7 days a week. All EMS providers perform cardiopulmonary resuscitation according to the Japanese cardiopulmonary resuscitation guidelines.[12] This study acquired prehospital resuscitation data from the All-Japan Utstein Registry of the Fire and Disaster Management Agency of Japan. We collected data corresponding to the Utstein-style international guidelines for reporting OHCA.[13] In Japan, the 2005 version[13] of the Utstein style has been used even after the version changes.

Data Collection and Quality Control

Details of the registry's data collection and quality control have been previously published.[7] For prehospital data collection and quality control, each EMS completed the data form by collaborating with the attending physician who was responsible for the patient. For in-hospital data, the CRITICAL registry collects comprehensive data on patients with OHCA after hospital arrival, details of which have been previously presented.[7] In the current registry, anonymized data were entered into a web form by medical staff members in cooperation with the attending physician. Prehospital and in-hospital data were uploaded into the registry system, systematically checked by a computer system, and verified by a working group of experts in emergency medicine, clinical epidemiology, and statistics.

Case Adjudication

We categorized the following causes for presumed SCDs and resuscitated patients with OHCAs (which included survivors and nonsurvivors of OHCA): the broader cause (cardiac or noncardiac), specific causes of cardiac origin (eg, acute coronary syndrome, other cardiac disease, and probable cardiac disease), and specific causes of noncardiac origin (eg, cerebral vascular disease, respiratory disease). Probable cardiac cause was used when all available data and workup revealed no evidence of a noncardiac cause. The categories of the noncardiac cause were based on the Utstein style,[13] which includes respiratory disease, cerebrovascular disease, and other cause. In the CRITICAL registry, adjudication of these causes was made by emergency physicians in charge of each institute considering clinical implications and clinical findings, including coronary angiography, computed tomography, laboratory tests, and other clinical tests. On the adjudication, the physician diagnoses a probable or specific disease in clinical setting, and this was categorized by research personnel in 1 of the aforementioned categories. Further details including the follow-up have been previously described.[7]

Statistical Analysis

Continuous variables are presented as mean±SD, and categorical variables are described as percentages. Patient characteristics and OHCA circumstances are described for presumed SCDs, survivors of OHCA, and nonsurvivors of OHCA. Patient characteristics and OHCA circumstances in survivors and nonsurvivors are compared using the chi-square or Wilcoxon rank-sum test. The main analysis of our study was to compare the proportion of the cardiac cause between the nonsurvivors and survivors of OHCA by the chi-square test. We also performed the same comparison for causes of cardiac arrest. In subgroup analyses, causes of OHCA for survivors and nonsurvivors were stratified by age: 18 to 35 years, 36 to 64 years, 65 to 79 years, and 80 to 90 years, as per our previous study.[14] There

were no missing data for the main analysis in the study. For prehospital data, the Utstein-style data collection in Japan is recorded as a mandatory task by emergency medical technicians at each fire department when they perform resuscitation on patients with OHCA. Therefore, if there are any missing values, they are fed back to the field during collection at the fire department or integration at the Fire and Disaster Management Agency, resulting in an almost completely missing-free database. On the other hand, for in-hospital data, which refer to data after transportation, the items presented in this paper are considered essential core items, and the input system is designed so that the case cannot be confirmed if there are missing values. If there are still any missing values, the CRITICAL study's core researchers check each case's missing value through the registry system, and the core researchers contact the responsible individuals at each hospital to ensure that no missing values remain. We detail the rate of the missing data in Table 1. All *P* values are 2 sided for statistical analysis, and statistical significance was set at $P<0.05$. All statistical analyses were performed using STATA version 16.0 SE software (Stata Corp LP, USA) and R version 4.4.0 (2024-04-24).

RESULTS

Figure 1 indicates an overview of the population in this study. Between January 1, 2012 and December 31, 2020 in Osaka, Japan, 21 100 cases of OHCA were included in the CRITICAL study via all participating EMS agencies. Patients without a resuscitation attempt in the emergency department (n=517) or prehospital data (n=1988), children aged <18 years (n=516), and older adults aged >91 years (n=941) were excluded. Of the remaining 17 138 patients with OHCA, 11 470 died in the emergency department; of these, 8005 presumed SCDs were included in the analysis after excluding patients with cancer (n=234) and OHCAs due to external causes (n=3231). The remaining 5668 patients with OHCA were resuscitated to hospital admission; among these, 69 had terminal cancer and 1352 had OHCAs due to external causes, leaving 4247 resuscitated patients with OHCAs included in the analysis. Of these, 1293 (30.4%) survived month after the event, and 2954 (69.6%) died within 1 month after the event. Survivors of OHCA accounted for 10.6% (1293/12252) of all OHCAs included in the registry during the study period.

Table 1 shows baseline characteristics with missing variables of 8005 presumed SCDs and 4247 resuscitated patients with OHCAs, the latter group further divided into nonsurvivors of OHCA (n=2954) and survivors of OHCA (n=1293). For presumed SCDs, mean age was 71.2 years (±14.1 years SD); only a small minority achieved return of spontaneous circulation before hospital arrival (n=86, 1.1%). The majority of presumed SCDs had asystole (n=4831, 60.4%) or pulseless electrical activity (n=2380, 29.7%) as the first documented rhythm at EMS arrival. Among the 4247 resuscitated patients with OHCAs, survivors were younger, more often male, and more often had achieved return of spontaneous circulation before hospital arrival. Survivors of OHCAs also more commonly had ventricular fibrillation/pulseless ventricular tachycardia as a first documented rhythm at EMS arrival and were more often witnessed, had received bystander-initiated cardiopulmonary resuscitation, or had received public-access automated external defibrillator shock.

Table 2 summarizes underlying causes of presumed SCDs and resuscitated patients with OHCAs (nonsurvivors and survivors). Among the presumed SCDs (n=8005), cardiac causes accounted for 6789 (84.8%) cases whereas noncardiac cause was found in 1216 patients (15.2%). The leading cause of presumed SCDs was probable cardiac disease (n=6184, 77.3%; Table 2). Among the resuscitated patients with OHCAs (n=4247), cardiac cause was found in 3110 patients (73.2%) and noncardiac cause was found in 1137 patients (26.8%; Table 2).

Among resuscitated patients with OHCAs, survivors were more likely to have cardiac cause than nonsurvivors (85.7% versus 67.8%; $P<0.001$, Figure 2). Acute coronary syndrome was the most common cause of OHCA among survivors (n=522, 40.4%; Table 2), and probable cardiac disease was the most common among nonsurvivors (n=1302, 44.1%; Table 2). Although cerebrovascular disease accounted for only 1.2% of survivors of OHCA, it accounted for 9.8% of nonsurvivors ($P<0.001$).

Cardiac causes accounted for more than two thirds of causes of presumed SCDs in each age category, with most of these probable (Table 3). Cerebrovascular disease was rare in survivors of OHCA but was the most common noncardiac cause among nonsurvivors of OHCA aged 36 to 64 years (n=144, 17.8%; Table 3). Respiratory disease accounted for >10% of causes among nonsurvivors and survivors in the oldest age group 80 to 90 years (n=98, 11.3%; n=26, 14.7%).

DISCUSSION

Before summarizing the results, we will clarify the definitions of the cases used in this study to avoid any potential misunderstandings. Based on the Lancet Commission's definition,[11] patients with OHCA were categorized as presumed SCDs if they died in the emergency department or as resuscitated OHCA if they initially survived resuscitation and were admitted to the hospital. This definition might lead to some confusion because the term SCD also encompasses cases

Table 1. Baseline Characteristics

	Presumed SCDs		Resuscitated patients with OHCAs				
			All	Nonsurvivor	Survivor		
	(n=8005)	Missing (%)	(n=4247)	(n=2954)	(n=1293)	Missing (%)	*P* value[†]
Age, y, mean±SD	71.2±14.1	0.0	67.8±14.9	69.7±14.4	63.3±15.1	0.0	<0.001
Age group, n (%)		0.0				0.0	<0.001
18–35 y	167 (2.1)		133 (3.1)	62 (2.1)	71 (5.5)		
36–64 y	1900 (23.7)		1342 (31.6)	810 (27.4)	532 (41.1)		
65–79 y	3223 (40.3)		1730 (40.7)	1217 (41.2)	513 (39.7)		
80–90 y	2715 (33.9)		1042 (24.5)	865 (29.3)	177 (13.7)		
Men, n (%)	5034 (62.9)	0.0	2901 (68.3)	1924 (65.1)	977 (75.6)	0.0	<0.001
Departure of ambulance or helicopter with physicians, n (%)	713 (8.9)	0.0	639 (15.1)	411 (13.9)	228 (17.6)	0.0	0.002
ROSC status, n (%)		0.0				0.0	<0.001
ROSC before hospital arrival	86 (1.1)		1120 (26.4)	386 (13.1)	734 (56.8)		
ROSC after hospital arrival	1005 (12.6)		2441 (57.5)	1931 (65.4)	510 (39.4)		
First documented rhythm at EMS arrival, n (%)		0.0				0.0	<0.001
VF/pulseless VT	555 (6.9)		1278 (30.1)	570 (19.3)	708 (54.8)		
PEA	2380 (29.7)		1377 (32.4)	1068 (36.2)	309 (23.9)		
Asystole	4831 (60.4)		1301 (30.6)	1170 (39.6)	131 (10.1)		
Others	239 (3)		291 (6.9)	146 (4.9)	145 (11.2)		
Witness status, n (%)		2.7				2.6	<0.001
Witnessed by family	1861 (23.3)		1443 (34)	995 (33.7)	448 (34.7)		
Citizens	493 (6.2)		595 (14)	307 (10.4)	288 (22.3)		
Witnessed by EMS personnel	646 (8.1)		581 (13.7)	390 (13.2)	191 (14.8)		
Not witnessed	5005 (62.5)		1628 (38.3)	1262 (42.7)	366 (28.3)		
Bystander-initiated cardiopulmonary resuscitation, n (%)	3353 (41.9)	0.0	1771 (41.7)	1176 (39.8)	595 (46)	0.0	<0.001
Shock by public-access automated external defibrillators, n (%)	68 (0.9)	0.0	198 (4.7)	57 (1.9)	141 (10.9)	0.0	<0.001
First documented rhythm at hospital arrival, n (%)		0.0				0.0	<0.001
VF/pulseless VT	260 (3.3)		543 (12.8)	292 (9.9)	251 (19.4)		
PEA	1669 (20.9)		1203 (28.3)	981 (33.2)	222 (17.2)		
Asystole	5985 (74.8)		1417 (33.4)	1293 (43.8)	124 (9.6)		
Others	91 (1.1)		1084 (25.5)	388 (13.1)	696 (53.8)		
Defibrillation by EMS, n (%)	1016 (12.7)	28.7	1516 (35.7)	743 (25.2)	773 (59.8)	18.4	<0.001
Advanced airway management, n (%)	3864 (48.3)	36.5	2030 (47.8)	1625 (55)	405 (31.3)	33.8	<0.001
Adrenaline administration, n (%)	1751 (21.9)	0.0	1258 (29.6)	981 (33.2)	277 (21.4)	0.0	<0.001
EMS response time (call to contact with the patient by EMS), min, mean±SD	9.8±5	0.0	10.1±5.8	9.56±5.7	10.3±5.9	0.0	<0.001
Call to prehospital ROSC, min, mean±SD*	23.8±9	96.8	19.4±8.8	23.1±8.7	16.5±7.8	64.8	<0.001
Call to in-hospital ROSC, min, mean±SD*	47.5±47.9	87.5	50.7±89.2	52.5±99.3)	43.8±26.4	42.8	<0.001

EMS indicates emergency medical services; OHCA, out-of-hospiral cardiac arrest; SCD, sudden cardiac death; ROSC, return of spontaneous circulation; PEA, pulseless electrical activity; VF, ventricular fibrillation; and VT, ventricular tachycardia.

*Call to prehospital ROSC and call to in-hospital ROSC were caluculated in the cases for which ROSC times were available.

[†]*P* value for comparing OHCA survivors with nonsurvivors.

of OHCA resulting from noncardiac causes. To mitigate this, the Lancet Commission suggested using the term "presumed SCD" for cases where the cause remains unconfirmed without autopsy, toxicology, or histological examination.[6] In line with this recommendation, we adopted the term "presumed SCDs." Furthermore, resuscitated patients with OHCA were subdivided into 2 groups: survivors of OHCA, who remained alive 1 month after the event, and nonsurvivors, who died in the hospital despite initially surviving to admission.

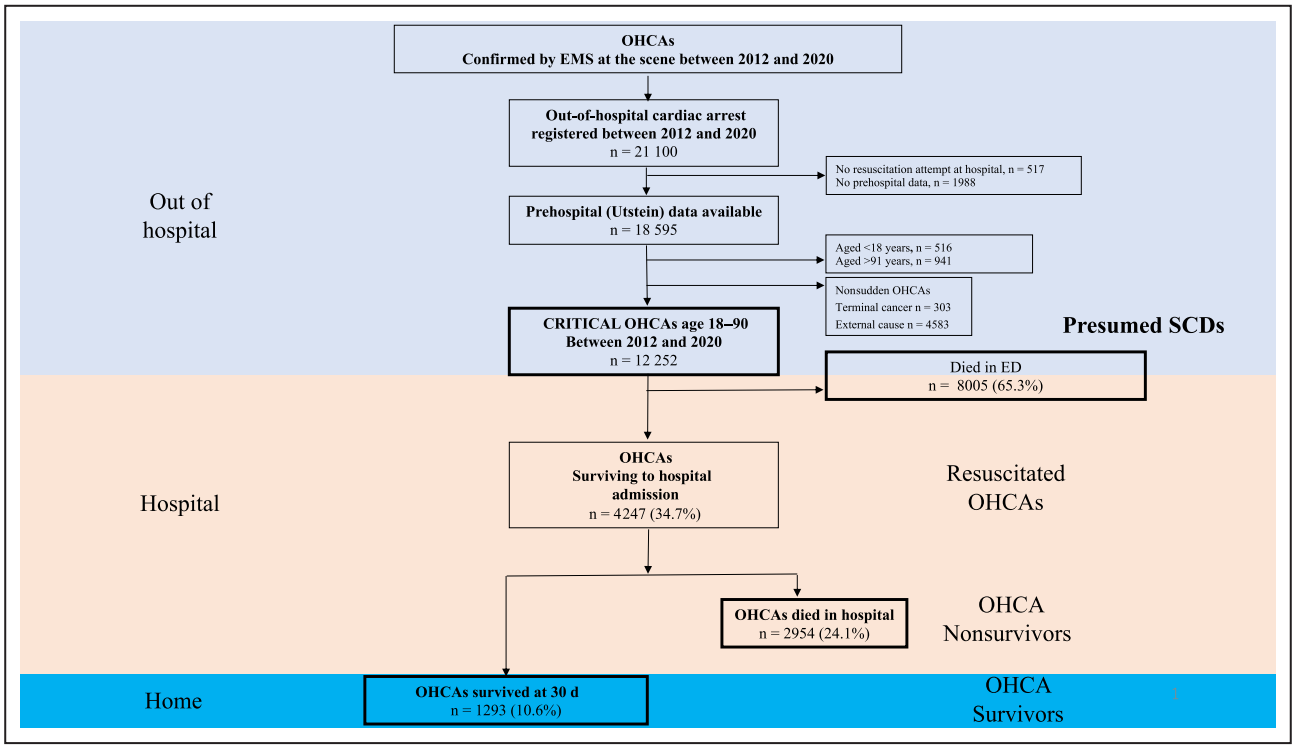

Figure 1. Patient flow.
Among the out-of-hospital cardiac arrest confirmed by emergency medical services at the scene between 2012 and 2020, 4247 patients were resuscitated out-of-hospital cardiac arrest. Of these, 1293 were survivors of OHCA, and 2954 were nonsurvivors of OHCA. Presumed sudden cardiac deaths totaled 8005 patients. ED indicates emergency department; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest; and SCD, sudden cardiac death.

In this 9-year study we investigated underlying cause stratified by survival outcome in consecutive patients with OHCA aged 18 to 90 years who received resuscitation attempts and were transported to participating institutions in Osaka, Japan. Because Japanese law dictates that all patients with OHCAs (resuscitated or not) must be transported to the emergency department, this study also captured the vast majority of incident out-of-hospital SCD. We found that three quarters of presumed SCDs had underlying cardiac cause, and among patients with OHCAs resuscitated to hospital admission, significantly more survivors than nonsurvivors of OHCA were cardiac in origin. These results suggest that fatal outcomes after initially resuscitated patients with OHCA are caused by more heterogeneous conditions than those who survive, including cerebrovascular disease (9.8%) and respiratory diseases (8.3%). Middle aged cases 36 to 64 years had the highest prevalence of cerebrovascular disease as underlying cause of OHCA.

Table 2. Causes of Presumed SCDs and Resuscitated Patients With OHCAs by Survival to Discharge, n (%)

	Presumed SCDs	Resuscitated patients with OHCAs			*P* value*
		Total	Nonsurvivors of OHCA	Survivors of OHCA	
Cause of arrest	(n=8005)	(n=4247)	(n=2954)	(n=1293)	
Cardiac, n %	6789 (84.8)	3110 (73.2)	2002 (67.8)	1108 (85.7)	<0.001
Acute coronary syndrome	228 (2.8)	955 (22.5)	433 (14.7)	522 (40.4)	
Other cardiac disease	377 (4.7)	626 (14.7)	267 (9)	359 (27.8)	
Probable cardiac disease	6184 (77.3)	1529 (36)	1302 (44.1)	227 (17.6)	
Noncardiac disease, n %					<0.001
Cerebrovascular disease	161 (2)	305 (7.2)	289 (9.8)	16 (1.2)	
Respiratory disease	194 (2.4)	324 (7.6)	245 (8.3)	79 (6.1)	
Others	861 (10.8)	508 (12)	418 (14.2)	96 (7.4)	

*Survivors of OHCA vs nonsurvivors. OHCA indicates out-of-hospital cardiac arrest; and SCD, sudden cardiac death.

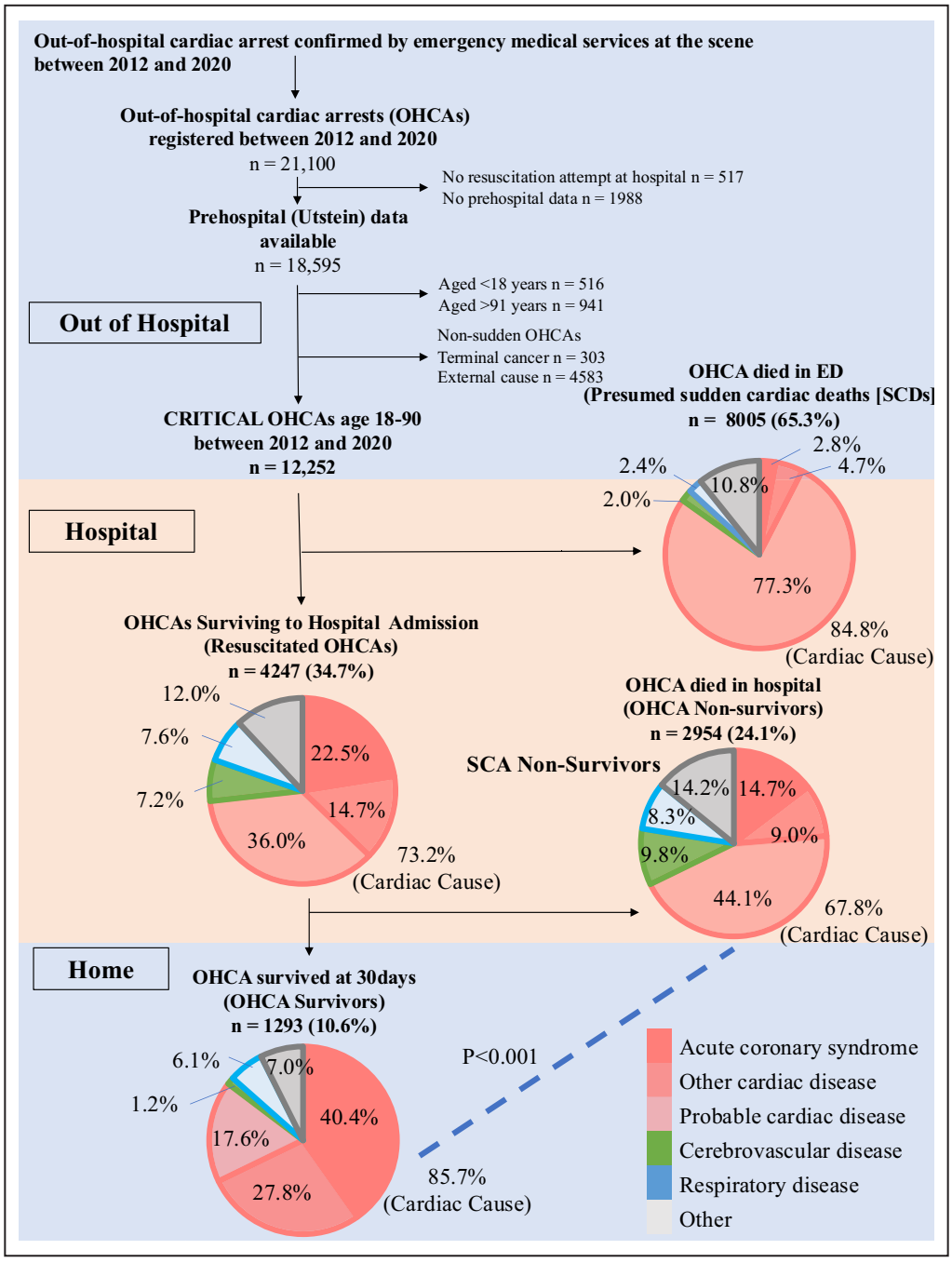

Figure 2. Central illustration.
Underlying causes of out-of-hospital cardiac arrest in CRITICAL study, Osaka, Japan. All OHCAs from July 1, 2012, to December 31, 2020, Osaka, Japan, were identified through EMS agencies. In Japan, all OHCAs must be transported to the ED where death is declared if resuscitation is unsuccessful; the latter group was considered presumed SCDs. Patients with OHCAs dying in the ED (SCDs) or with nonsudden OHCAs (terminal cancer and external causes) were excluded, to include patients with OHCAs resuscitated to hospitalization. Causes were probable when determined only by attending physician impression or confirmed when autopsy or postresuscitation hospital workup was performed: cardiac cause including acute coronary syndrome, other cardiac cause, and probable cardiac cause (red), cerebrovascular disease(green), respiratory disease (blue), or other (gray) cause. Cardiac causes accounted for 84.8% (6789 of 8005) of presumed SCDs. Cardiac causes accounted for 84.8% (1108 of 1293) of survivors of OHCA, significantly higher than the 55.8% of nonsurvivors (2002 of 2954; $P<0.001$). Cerebrovascular disease was significantly more common in nonsurvivors than survivors (9.8% vs 1.2%; $P<0.001$). CRITICAL indicates Comprehensive Registry of In-Hospital Intensive Care for OHCA Survival; ED, emergency department; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest; and SCD, sudden cardiac death.

Table 3. Causes of Presumed Sudden Cardiac Deaths and Resuscitated Out-of-Hospital Cardiac Arrests by Age, n (%)

	Total	18–35 y	36–64 y	65–79 y	80–90 y
Causes of arrest of presumed SCDs	(n=8005)	(n=167)	(n=1900)	(n=3223)	(n=2715)
Cardiac	6789 (84.8)	136 (81.4)	1570 (82.6)	2751 (85.4)	2332 (85.9)
Acute coronary syndrome	228 (2.8)	4 (2.4)	74 (3.9)	95 (2.9)	55 (2.0)
Other cardiac disease	377 (4.7)	6 (3.6)	65 (3.4)	191 (5.9)	115 (4.2)
Probable cardiac disease	6184 (77.3)	126 (75.4)	1431 (75.3)	2465 (76.5)	2162 (79.6)
Noncardiac disease	1216 (15.2)	31 (18.6)	330 (17.4)	472 (14.6)	383 (14.1)
Cerebrovascular disease	161 (2.0)	2 (1.2)	74 (3.9)	53 (1.6)	32 (1.2)
Respiratory disease	194 (2.4)	4 (2.4)	37 (1.9)	79 (2.5)	74 (2.7)
Others	861 (10.8)	25 (15)	219 (11.5)	340 (10.5)	277 (10.2)
Causes of arrest of resuscitated patients with OHCAs					
All resuscitated patients with OHCAs	(n=4247)	(n=133)	(n=1342)	(n=1730)	(n=1042)
Cardiac	3110 (73.2)	107 (80.5)	986 (73.5)	1272 (73.5)	745 (71.5)
Acute coronary syndrome	955 (22.5)	8 (6.0)	414 (30.8)	423 (24.5)	110 (10.6)
Other cardiac disease	626 (14.7)	54 (40.6)	238 (17.7)	238 (13.8)	96 (9.2)
Probable cardiac disease	1529 (36.0)	45 (33.8)	334 (24.9)	611 (35.3)	530 (50.9)
Noncardiac disease	1137 (26.8)	26 (19.5)	356 (26.5)	458 (26.5)	297 (28.5)
Cerebrovascular disease	305 (7.2)	7 (5.3)	153 (11.4)	106 (6.1)	39 (3.7)
Respiratory disease	324 (7.6)	3 (2.3)	58 (4.3)	139 (8.0)	124 (11.9)
Others	508 (12)	16 (12)	145 (10.8)	213 (12.3)	134 (12.9)
Resuscitated nonsurvivors of OHCAs	(n=2954)	(n=62)	(n=810)	(n=1217)	(n=865)
Cardiac	2002 (67.8)	43 (69.4)	512 (63.2)	830 (68.2)	617 (71.3)
Acute coronary syndrome	433 (14.7)	2 (3.2)	170 (21.0)	191 (15.7)	70 (8.1)
Other cardiac disease	1138 (26.8)	13 (21.0)	83 (10.2)	115 (9.4)	56 (6.5)
Probable cardiac disease	1302 (44.1)	28 (45.2)	259 (32.0)	524 (43.1)	491 (56.8)
Noncardiac disease	952 (32.2)	19 (30.6)	298 (36.8)	387 (31.8)	248 (28.7)
Cerebrovascular disease	289 (9.8)	6 (9.7)	144 (17.8)	101 (8.3)	38 (4.4)
Respiratory disease	245 (8.3)	3 (4.8)	37 (4.6)	107 (8.8)	98 (11.3)
Others	418 (14.2)	10 (16.1)	117 (14.4)	179 (14.7)	112 (12.9)
Resuscitated survivors of OHCAs	(n=1293)	(n=71)	(n=532)	(n=513)	(n=177)
Cardiac	1108 (85.7)	64 (90.1)	474 (89.1)	442 (86.2)	128 (72.3)
Acute coronary syndrome	522 (40.4)	6 (8.5)	244 (45.9)	232 (45.2)	40 (22.6)
Other cardiac disease	359 (27.8)	41 (57.7)	155 (29.1)	123 (24.0)	40 (22.6)
Probable cardiac disease	227 (17.6)	17 (23.9)	75 (14.1)	87 (17.0)	48 (27.1)
Noncardiac disease	185 (14.3)	7 (9.9)	58 (10.9)	71 (13.8)	49 (27.7)
Cerebrovascular disease	16 (1.2)	1 (1.4)	9 (1.7)	5 (1.0)	1 (0.6)
Respiratory disease	79 (6.1)	0 (0)	21 (3.9)	32 (6.2)	26 (14.7)
Others	90 (7.0)	6 (8.5)	28 (5.3)	34 (6.6)	22 (12.4)

OHCA indicates out-of-hospital cardiac arrest; and SCD, sudden cardiac death.

Although a meta-analysis has summarized that OHCA may not be due to cardiac disease, with higher survival of patients with a cardiac cause of the OHCA,[15] the definitions of the SCD or arrest were vastly different in each included study. Moreover, although a previous report in Japan[16] indicated that 21% of OHCAs were due to cerebral and respiratory cause, a crude definition of OHCA was used. In this study, as per the convention of recent reports by Tseng et al.[4,5] and a report by the Lancet committee[11] that used conventional definitions of OHCA, presumed SCD, and SCD,[10,17] we separated outcomes after OHCAs by lethality: presumed SCDs versus OHCA resuscitated to hospital admission, then the latter group into nonsurvivors and survivors to hospital discharge; the use of a single standardized definition will facilitate comparison of our result in Osaka, Japan with international registries.

Death after OHCA is frequently considered synonymous with SCD or sudden death, and the outcomes

of OHCA and SCD or sudden death are used interchangeably.[11] Tseng et al demonstrated that SCDs (ie, those who died in the field or emergency department), sudden cardiac arrest (SCA) (ie, those who were resuscitated and treated in the hospital) which is close to survivors of OHCA in our study, survivors of SCA, and nonsurvivors of SCA (those who died in hospital after initial resuscitation) are substantially different conditions, as nearly half of lethal cases (presumed SCDs and nonsurvivors of SCA) were caused by underlying nonarrhythmic and noncardiac conditions; "cardiac cause" includes "cardiac arrhythmic" (ie acute coronary artery diseases and cardiomyopathy) and "cardiac nonarrhythmic" (ie tamponade and acute heart failure), whereas 98% of survivors of SCA had confirmed cardiac causes.[4,5] Our results confirm the findings in San Francisco County, and because we also report that only 10% of all patients with OHCAs in Osaka, Japan were alive at 1 month after the event, further inroads into reducing the overall burden of sudden death and improving persistently poor survival outcomes after OHCA may require a refinement of current resuscitation strategies to rescue the substantial minority which are due to noncardiac causes, including investigation and earlier recognition of nonischemic and nonarrhythmic causes. Although there were few comprehensive pathogenetic studies like the one in San Francisco, some of the previous studies on pathogenesis might support our results. For example, it was reported that coronary heart disease accounts for up to 70% of cases in the Western world,[18] but these references did not consider the difference between survivors and nonsurvivors. On the other hand, in a study in France, among young patients with presumed OHCA (<45 years) who were admitted to the intensive care unit, nonsurvivors had a lower proportion of cardiac causes (54.5% versus 89.0%) but a higher proportion of neurologic causes (19.3% versus 3.9%) compared with survivors.[19] Also, for the hospitalized patients with OHCA (survivors of OHCA in our study), the proportion of cardiac causes (73.2%) was similar to the number (65.5%) in a study in France that reviewed the pathogenetic diagnoses of patients with OHCA admitted to the intensive care unit.[20]

Our study also confirms prior reports that resuscitated OHCAs due to underlying cerebrovascular disease are highly lethal,[4] as very few of these cases survived. Few studies have investigated the prognosis of OHCAs due to cerebrovascular disease such as subarachnoid hemorrhage, but the San Francisco study[5] reported that of the nearly 1 in 5 resuscitated patients with SCAs due to underlying neurologic emergencies, none survived. This is similar to the results of a small study in Japan that reported none of the recognized cases due to cerebrovascular disease survived to hospital discharge.[6,17] Furthermore, previous study which investigated the outcome of OHCA caused by stroke by using Utstein registry in Japan reported that stroke (cerebrovascular disease)-related OHCA had lower 1-month survival rates and poorer neurological outcomes than cardiogenic OHCA.[21] The study did not investigate the proportion of the OHCA due to cerebrovascular disease among all of the nontraumatic OHCA so that the clinical burden to the each generation was not clear, but the current study revealed that cerebrovascular disease accounted for almost one fifth of middle-aged cases, which suggests the need for earlier recognition and targeted prevention strategy in this age group.

The high prevalence of "probable cardiac disease" among sudden death and nonsurvivors of OHCA aged 18 to 35 years in this study also suggests that a more aggressive search for causes is needed in these age groups. In the past literature, "coronary heart disease" and "structural heart disease" were the most common reasons for "probable cardiac causes" (ie, no apparent causes) among young adults.[22] However, most probable or presumed cardiac causes in young adults were found to be actually due to noncardiac causes.[23] Thus future studies of all OHCAs may benefit from a more in-depth examination of underlying cause of apparent cardiac arrest, by clarifying probable causes, with the goal of developing specific preventive strategies for each underlying cause.

Limitations

This study has several limitations. First, we did not use World Health Organization criteria to define suddenness in the CRITICAL study.[24] This selection bias might have affected the causes of presumed SCDs or nonsurvivors of OHCA to include non-SCAs, such as cardiac arrest from renal diseases or aspiration pneumonia following the progression of dementia. However, we excluded OHCAs in patients with terminal conditions such as cancer. Second, probable diagnoses were used in the CRITICAL study, especially in presumed SCDs, which may lead to misclassification of causes in this group as presumed SCDs are not routinely evaluated postmortem in Japan. In the CRITICAL study, more complete examinations, including CT, were performed in hospitalized cases after resuscitated OHCA as compared with presumed SCDs thus the certainty of underlying causes is greater in the former, although the rate of diagnostic tests such as computed tomography or specific blood tests was not recorded in the registry.

Additionally, in the population of patients with OHCA who died before reaching the hospital (presumed SCDs), the cause in most cases was adjudicated without examinations such as autopsy. Therefore, in this study, we determined the cause of arrest (cardiac

or noncardiac) based on the "Utstein-style" recommendation for the registry of OHCAs,[25] the international guideline for analyzing and comparing data on OHCAs. In the Utstein style, the arrest is presumed to be of cardiac origin unless it is caused by noncardiac causes such as cerebrovascular diseases, respiratory diseases, and trauma, with the diagnoses of cardiac or noncardiac origin being clinically made. The "Utstein style" is universal and feasible, and we believe that it is the best way to analyze data on OHCAs in the moment despite its epidemiological limitations. Although we concluded that the frequency of noncardiac causes is higher among nonsurvivors than survivors of OHCA, cardiac causes were more common than noncardiac causes. This was especially true for probable cardiac causes, which might reflect that some probable causes were not well evaluated in the emergency department, and systematic diagnosis for this population might change the epidemiology of the causes.

Approximately three fourths of presumed SCDs in our study were probably due to unknown or incomplete postmortem workup, whereas the POST SCD study in San Francisco[4] used autopsy in almost all cases to demonstrate that only 60% of World Health Organization-defined sudden cardiac deaths, that is, patients with OHCAs dying in the field and declared cardiac in the field by EMS, were actually due to cardiac causes. In contrast, few lethal cases in the current study (presumed SCDs and nonsurvivors of OHCA) were confirmed by autopsy because in Japan, autopsies are extremely rare outside of forensic cases such as homicide or suicide.[26] Postmortem imaging such as computed tomography examinations are much more common in Japan than in other countries,[27] but the number of cases receiving postmortem computed tomography imaging in the current study is unknown, as the criteria for autopsy imaging varied by the institute. Thus, in many presumed SCDs, cardiac cause could be considered only probable. However, misclassification may be lower than other jurisdictions becayse nearly all presumed SCDs in Japan are still transported to the emergency department (rather than declared deceased in the field), thus even presumed SCDs receive at least partial medical examinations in the emergency department and therefore underlying causes of presumed SCDs this report are "less probable" than in other studies. Furthermore, this registry lacks detailed data on the specific pathogenesis of respiratory, cardiac, and neurological causes beyond what is described in our paper.

Another limitation was that we included only the patients who were transported to the emergency centers in the CRITICAL study, which accounts for about one third of the population with OHCA in Osaka; this might introduce bias in the current study.

Finally, selection bias is possible because it was conducted in emergency centers in metropolitan areas in Japan, and our study captured approximately one quarter of all incident OHCAs in Osaka during the study period. Furthermore, the diagnostic practice is different between the institutions. Despite these limitations, this study is meaningful because it describes the underlying causes of OHCA in an entire major metropolitan area of Japan, with a comparable underlying distribution of causes of resuscitated OHCA to prior studies. However, the results of our study may not be generalizable to other countries or regions due to variations in emergency care systems and protocols, even among industrialized nations.

CONCLUSIONS

In this 9-year study of underlying causes of OHCA in Osaka, Japan, underlying cardiac cause (probable and confirmed) was more common in survivors of OHCA than presumed SCDs and nonsurvivors of OHCA. Causes in nonsurvivors of OHCA were more heterogenous than in survivors of OHCA, including cerebrovascular diseases. Identifying the underlying causes of cardiac arrest and early detection and prevention of nonarrhythmic OHCA, including cerebrovascular disease especially in middle-aged adults, may improve persistently poor survival rates after OHCA.

ARTICLE INFORMATION

Received June 4, 2024; accepted January 15, 2025.

Affiliations

Department of Preventive Services, Kyoto University School of Public Health, Kyoto, Japan (S.Y., Y.O., N.N., S.K., S.K., Y.M., T.I.); Section of Cardiac Electrophysiology, Division of Cardiology, Department of Medicine, University of California-San Francisco, San Francisco, CA (Z.H.T.); Emergency and Critical Care Medical Center, Osaka Keisatsu Hospital, Osaka, Japan (T.Y.); Department of Traumatology and Acute Critical Medicine, Osaka University Graduate School of Medicine, Suita, Japan (S.N.); Department of Emergency and Critical Care Medicine, Kansai Medical University, Takii Hospital, Moriguchi, Japan (K.Y.); Department of Emergency Medicine, Tane General Hospital, Osaka, Japan (C.P.); Department of Critical Care Medicine, Osaka City University, Osaka, Japan (T.N.); Department of Emergency and Critical Care Medicine, Kindai University School of Medicine, Osaka-Sayama, Japan (T.I.); Department of Emergency and Critical Care, Medicine Osaka Medical and Pharmaceutical University, Takatsuki, Japan (K.Y.); Critical Care and Trauma Center, Osaka General Medical Center, Osaka, Japan (T.K.); Osaka Prefectural Nakakawachi Medical Center of Acute Medicine, Higashi-Osaka, Japan (M.K.); Senshu Trauma and Critical Care Center, Osaka, Japan (K.N.); Senri Critical Care Medical Center, Saiseikai Senri Hospital, Suita, Japan (Y.I.); Traumatology and Critical Care Medical Center, National Hospital Organization Osaka National Hospital, Osaka, Japan (T.S.); Emergency and Critical Care Medical Center, Osaka City General Hospital, Osaka, Japan (T.M.); Department of Pediatrics, Osaka Red Cross Hospital, Osaka, Japan (H.S.); Emergency and Critical Care Medical Center, Kishiwada Tokushukai Hospital, Osaka, Japan (Y.H.); Department of Emergency and Critical Care Medicine, Kansai Medical University, Hirakata, Osaka, Japan (A.O.); Department of Emergency Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan (T.M.); Division of Emergency Medicine, Hyogo Prefectural Kobe Children's Hospital, Kobe, Japan (S.M.); Division of Environmental Medicine and Population Sciences, Department of Social and Environmental Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan (L.Z., T.K.); and Department of Food Science, Otsuma Women's University, Tokyo, Japan (K.K.).

Acknowledgments

We appreciate all emergency medical service personnel for collecting the Utstein data and Ms. Ikuko Nakamura and Yumi Murai for supporting our study. Furthermore, we thank the CRITICAL study group, POST SCD study members, and all the personnel at the participating institutions for their contributions.

Sources of Funding

This study was supported by a scientific research grant from the JSPS KAKENHI of Japan (22H03313 to Iwami and 22K09139 to Kitamura). Dr Tseng was supported by grants from the Centers for Disease Control and Prevention (6 NU38DP000019-01-01) and National Institutes of Health/National Heart, Lung, and Blood Institute (R01HL147035 and R01HL157247). All other authors have reported that they have no relationships relevant to the contents of this paper.

Disclosures

None.

REFERENCES

1. Current status of emergency rescue. Accessed August 26, 2024. https://www.fdma.go.jp/publication/rescue/.
2. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Delling FN, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. *Circulation*. 2020;141:e139–e596. doi: 10.1161/CIR.0000000000000757
3. Okubo M, Kiyohara K, Iwami T, Callaway CW, Kitamura T. Nationwide and regional trends in survival from out-of-hospital cardiac arrest in Japan: a 10-year cohort study from 2005 to 2014. *Resuscitation*. 2017;115:120–128. doi: 10.1016/j.resuscitation.2017.03.036
4. Tseng ZH, Olgin JE, Vittinghoff E, Ursell PC, Kim AS, Sporer K, Yeh C, Colburn B, Clark NM, Khan R, et al. Prospective countywide surveillance and autopsy characterization of sudden cardiac death: POST SCD study. *Circulation*. 2018;137:2689–2700. doi: 10.1161/CIRCULATIONAHA.117.033427
5. Ricceri S, Salazar JW, Vu AA, Vittinghoff E, Moffatt E, Tseng ZH. Factors predisposing to survival after resuscitation for sudden cardiac arrest. *J Am Coll Cardiol*. 2021;77:2353–2362. doi: 10.1016/j.jacc.2021.03.299
6. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M; STROBE Initiative. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18:805–835. doi: 10.1016/j.ijsu.2014.07.014
7. Yamada T, Kitamura T, Hayakawa K, Yoshiya K, Irisawa T, Abe Y, Ishiro M, Uejima T, Ohishi Y, Kaneda K, et al. Rationale, design, and profile of comprehensive registry of in-hospital intensive care for OHCA survival (CRITICAL) study in Osaka, Japan. *J Intensive Care Med*. 2016;4:10. doi: 10.1186/s40560-016-0128-5
8. Statistics Bureau, Ministry of Internal Affairs, Communications. Statistics Bureau Home Page. Accessed August 26, 2024. https://www.stat.go.jp/english/.
9. FDMA:: Fire and Disaster Management Agency. Accessed August 4, 2023. https://www.fdma.go.jp/en/post1.html
10. McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, Sasson C, Crouch A, Perez AB, Merritt R, et al. Out-of-hospital cardiac arrest surveillance—cardiac arrest registry to enhance survival (CARES), United States, October 1, 2005–December 31, 2010. *MMWR Surveill Summ*. 2011;60:1–19.
11. Marijon E, Narayanan K, Smith K, Barra S, Basso C, Blom MT, Crotti L, D'Avila A, Deo R, Dumas F, et al. The lancet commission to reduce the global burden of sudden cardiac death: a call for multidisciplinary action. *Lancet*. 2023;402:883–936. doi: 10.1016/S0140-6736(23)00875-9
12. Kojima S, Nishihira K, Takegami M, Nakao YM, Honda S, Takahashi J, Takayama M, Shimokawa H, Sumiyoshi T, Ogawa H, et al. Nationwide real-world database of 20,462 patients enrolled in the Japanese acute myocardial infarction registry (JAMIR): impact of emergency coronary intervention in a super-aging population. *Int J Cardiol Heart Vasc*. 2018;20:1–6. doi: 10.1016/j.ijcha.2018.06.003
13. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, Cassan P, Coovadia A, D'Este K, Finn J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). *Resuscitation*. 2004;63:233–249. doi: 10.1161/01.CIR.0000147236.85306.15
14. Yoshimura S, Hirayama A, Kiguchi T, Irisawa T, Yamada T, Yoshiya K, Park C, Nishimura T, Ishibe T, Yagi Y, et al. Trends in in-hospital advanced management and survival of out-of-hospital cardiac arrest among adults from 2013 to 2017–a multicenter, prospective registry in Osaka, Japan. *Circ J*. 2021;85:1851–1859. doi: 10.1253/circj.CJ-20-1022
15. Carter RM, Cone DC. When is a cardiac arrest non-cardiac? *Prehosp Disaster Med*. 2017;32:523–527. doi: 10.1017/S1049023X17006446
16. Nagao K. Out-of-hospital cardiac arrest related to cardiac etiology and the weather. *Circ J*. 2013;77:1988–1989. doi: 10.1253/circj.cj-13-0675
17. Al-Khatib SM, Yancy CW, Solis P, Becker L, Benjamin EJ, Carrillo RG, Ezekowitz JA, Fonarow GC, Kantharia BK, Kleinman M, et al. 2016 AHA/ACC clinical performance and quality measures for prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association task force on performance measures. *Circ Cardiovasc Qual Outcomes*. 2017;10:e000022. doi: 10.1161/HCQ.0000000000000022
18. Wong CX, Brown A, Lau DH, Chugh SS, Albert CM, Kalman JM, Sanders P. Epidemiology of sudden cardiac death: global and regional perspectives. *Heart Lung Circ*. 2019;28:6–14. doi: 10.1016/j.hlc.2018.08.026
19. Sharifzadehgan A, Gaye B, Bougouin W, Narayanan K, Dumas F, Karam N, Rischard J, Plu I, Waldmann V, Algalarrondo V, et al. Lack of early etiologic investigations in young sudden cardiac death. *Resuscitation*. 2022;179:197–205. doi: 10.1016/j.resuscitation.2022.06.023
20. Geri G, Passouant O, Dumas F, Bougouin W, Champigneulle B, Arnaout M, Chelly J, Chiche J-D, Varenne O, Guillemet L, et al. Etiological diagnoses of out-of-hospital cardiac arrest survivors admitted to the intensive care unit: insights from a French registry. *Resuscitation*. 2017;117:66–72. doi: 10.1016/j.resuscitation.2017.06.006
21. Fukuda T, Ohashi-Fukuda N, Kondo Y, Sera T, Doi K, Yahagi N. Epidemiology, risk factors, and outcomes of out-of-hospital cardiac arrest caused by stroke: a population-based study. *Medicine (Baltimore)*. 2016;95:e3107. doi: 10.1097/MD.0000000000003107
22. Allan KS, Morrison LJ, Pinter A, Tu JV, Dorian P; Rescu Investigators. Unexpected high prevalence of cardiovascular disease risk factors and psychiatric disease among young people with sudden cardiac arrest. *J Am Heart Assoc*. 2019;8:e010330.
23. Allan KS, Morrison LJ, Pinter A, Tu JV, Dorian P; Rescu Epistry Investigators. Presumed cardiac arrest in children and young adults: a misnomer? *Resuscitation*. 2017;117:73–79.
24. World Health Organization (WHO). In: World Health Organization, ed *Sudden cardiac death*. Genève: Switzerland; 1985:1–25.
25. Cummins RO, Chamberlain DA, Abramson NS, Allen M, Baskett PJ, Becker L, Bossaert L, Delooz HH, Dick WF, Eisenberg MS. Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style. A statement for health professionals from a task force of the American Heart Association, the European Resuscitation Council, the Heart and Stroke Foundation of Canada, and the Australian Resuscitation Council. *Circulation*. 1991;84:960–975. doi: 10.1161/01.CIR.84.2.960
26. Maeda S, Kamishiraki E, Starkey J, Ikeda N. Why are autopsy rates low in Japan? Views of ordinary citizens and doctors in the case of unexpected patient death and medical error. *J Healthc Risk Manag*. 2013;33:18–25. doi: 10.1002/jhrm.21114
27. Yamashita Y, Murayama S, Okada M, Watanabe Y, Kataoka M, Kaji Y, Imamura K, Takehara Y, Hayashi H, Ohno K, et al. The essence of the Japan Radiological Society/Japanese College of Radiology Imaging Guideline. *Jpn J Radiol*. 2016;34:43–79. doi: 10.1007/s11604-015-0499-x