Available online at www.sciencedirect.com

Resuscitation Plus

journal homepage: www.elsevier.com/locate/resuscitation-plus

Clinical paper

Impact of defibrillation with automated external defibrillator by bystander before defibrillation by emergency medical system personnel on neurological outcome of out-of-hospital cardiac arrest with non-cardiac etiology

Akira Komori [a,b,c,*], *Hiroki Iriyama* [a,b,c], *Toshikazu Abe* [a,c]

Abstract

Aim of the study: Although defibrillation using automated external defibrillator (AED) by bystander prior to emergency medical system (EMS) arrival was associated with favorable outcomes in out-of-hospital cardiac arrest (OHCA) of cardiac cause, whether it improves outcomes of OHCA due to non-cardiac cause is not clear. We aimed to investigate the impact of defibrillation with AED by bystander before defibrillation by EMS personnel on the outcomes of OHCA of presumed non-cardiac cause.

Methods: This was a retrospective cohort study using the All-Japan Utstein registry (reference period: 2013 to 2017). We included adult patients with OHCA of presumed non-cardiac cause, who had initial shockable rhythm, and who received witnessed arrest bystander cardiopulmonary resuscitation (CPR). Exposure variable was defibrillation with AED by bystander in comparison with initial defibrillation by EMS. Logistic regression analyses were conducted to assess the association between bystander AED shock and favorable neurological outcome (Cerebral Performance Category scale 1 or 2) at one month.

Results: Among the 1,053 patients included for analysis, 57 (5.4%) received bystander AED shock. There was no statistically significant difference in the rate of favorable neurological outcome at one month between groups [9 (15.8%) vs 109 (10.9%), p = 0.26]. Logistic regression analysis adjusted for characteristics, intervention, and time course of CPR showed no association between bystander AED shock and favorable neurological outcome [OR (95% CI): 1.63 (0.70–3.77), p = 0.25].

Conclusion: In this study, defibrillation with AED by bystander before defibrillation by EMS personnel was not associated with the favorable outcomes of OHCA of presumed non-cardiac cause.

Keywords: Out-of-hospital cardiac arrest, Automated external defibrillator, Defibrillation, Non-cardiac cause, Favorable neurological outcome

Introduction

Early defibrillation in out-of-hospital cardiac arrest (OHCA) is associated with better outcomes.[1] Patients with OHCA have a better prognosis when the initial heart rhythm is shockable, and when early cardiopulmonary resuscitation (CPR) and rapid defibrillation are available.[2–4] Each minute of delay in defibrillation significantly reduces the survival in patients with shockable OHCA.[5] Hence, widespread availability of automated external defibrillator (AED) in the community has improved survival from OHCA,[3,6–9] as it decreases time to defibrillation by bystander in comparison with that by emergency medical system (EMS).

Although earlier defibrillation with AEDs by bystander before defibrillation by EMS personnel was associated with favorable neurological outcomes in patients with OHCA due to cardiac etiology, it is

* Corresponding author at: Department of Emergency and Critical Care Medicine, Tsukuba Memorial Hospital, 1187-299, Kaname, Tsukuba, Ibaraki 300-2622, Japan.

E-mail addresses: akg_6412@yahoo.co.jp (A. Komori), iriyamahiroki@yahoo.co.jp (H. Iriyama), abetoshi111@gmail.com (T. Abe).

https://doi.org/10.1016/j.resplu.2023.100363

Received 17 January 2023; Received in revised form 20 January 2023; Accepted 23 January 2023

unclear whether it also has a favorable impact on outcomes in patients with OHCA due to non-cardiac etiology. Studies have shown differences in the characteristics and prognosis of OHCA in patients with cardiac cause and those with non-cardiac cause.[10–13] Indeed, previous studies showing effectiveness of early defibrillation excluded OHCA patients with non-cardiac causes from their analyses and there is paucity of data of early defibrillation with AEDs for OHCA due to non-cardiac causes.[1,3,6–9] Evaluating the differences in the effectiveness of early defibrillation for OHCA divided into groups by the underlying etiology may help reconfirm the clinical significance of defibrillation in resuscitation strategy.

Therefore, we aimed to investigate the impact of defibrillation with AEDs by bystander before defibrillation by EMS personnel on the outcomes of OHCA of presumed non-cardiac cause.

Methods

Study design and data source

This was a retrospective cohort study using data from the All-Japan Utstein registry between 2013 and 2017. The registry is an ongoing, prospective, nationwide, population-based registry of all patients with OHCA in Japan, launched by the Fire and Disaster Management Agency (FDMA) from January 2005.

The EMS in Japan

In Japan, the FDMA supervises the national emergency system, and the local emergency system operates under the aegis of the local fire department. Calls to the universal emergency call number 119 are directly connected to the dispatch center of the local fire department. All EMS personnel are trained in performing CPR according to the Japanese CPR guidelines.[15] EMS personnel can use several resuscitation methods including defibrillation with an AED, insertion of a supraglottic airway device, insertion of a peripheral intravenous line, and administration of Ringer's lactate solution. In the field, only specially trained emergency lifesaving technicians are permitted to insert a tracheal tube and administer intravenous adrenaline under the supervision of an online physician. EMS personnel in Japan are legally prohibited from terminating CPR in the field unless return of spontaneous circulation (ROSC) is confirmed. Therefore, almost all patients with OHCA in Japan are transported to hospitals, except for those with obvious signs of death.

Data collection

With the cooperation of the physician, data pertaining to all OHCA patients were collected by EMS personnel at each local center using the Utstein-style template. Cause of cardiac arrest and outcomes such as one-month survival and one-month neurological outcome were also included.

Study participants

The inclusion criteria were: patients aged $\geq$ 18 years with OHCA of presumed non-cardiac causes; patients with initial shockable rhythm defined as ventricular fibrillation or pulseless ventricular tachycardia; patients who received witnessed arrest bystander CPR. The exclusion criteria were > 60 minutes elapsed from witnessed arrest to first defibrillation and > 60 minutes elapsed from witnessed arrest to arrival at hospital. We also excluded patients for whom the reported time variables were implausible.

Definitions

Exposure variable was defibrillation with AED by bystander in comparison with the initial defibrillation by EMS. Defibrillation with AEDs by bystander was defined as any shock delivered by a bystander-applied AED before EMS arrival. Defibrillation by EMS personnel was defined as initial shock delivered by EMS. The person who performed the basic CPR or defibrillation using a public access AED was defined as a bystander. Cardiac arrest was defined as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation. Cardiac arrest of presumed non-cardiac cause was defined when it was neither clearly cardiogenic nor there was any evidence to suggest cardiac etiology. Non-cardiac causes were grouped as follows: cerebrovascular diseases; respiratory diseases; malignancy; external factors; toxication; drowning; traffic accident; hypothermia; anaphylaxis; and others, in accordance with registry definition. No detailed information on the specific disease that caused the cardiac arrest was registered. The final diagnosis was made by the physician-in-charge as part of the clinical patient management. Neurological outcome was defined using the Cerebral Performance Category (CPC) scale: category 1, good cerebral performance; category 2, moderate cerebral disability; category 3, severe cerebral disability; category 4, coma or vegetative state; and category 5, death. The scoring on CPC scales was determined by the physician-in-charge. The primary outcome was favorable neurological outcome (CPC 1 or 2) at one month.

Statistical analysis

Continuous variables were presented as median and interquartile range, and categorical variables were presented as frequency and percentage. Continuous variables were compared using the Mann–Whitney U test and categorical variables were compared using the Chi-squared test.

We categorized the study participants into the following two groups: bystander AED and EMS shock groups. The former consisted of patients who received defibrillation with AED by a bystander, and the latter consisted of patients who received defibrillation via EMS. We compared characteristics such as sex and time course from witnessed arrest to each subsequent event, intervention such as resuscitation techniques by EMS personnel, and outcomes between the bystander AED shock group and EMS shock group. Then, logistic regression analyses were conducted to assess the association between bystander AED shock before EMS shock and outcomes. Logistic regression models were adjusted for the following variables based on clinical relevance and previous studies[2,7,15]: age, sex, number of deliveries of defibrillation, administration of adrenaline, time from witnessed arrest to initiation of bystander CPR, time from witnessed arrest to first defibrillation by EMS personnel, time from witnessed arrest to EMS personnel's contact with patients, and time from witnessed arrest to arrival at the hospital.

Two-sided p values < 0.05 were considered indicative of statistical significance. Statistical analyses were performed using Stata software, version 15.1 (Stata Corp, College Station, TX, USA).

Ethical Approval and consent to participate

The study protocol was approved by the Research Ethics Committee of the Tsukuba Memorial Hospital (IRB No. R04-10–01). Given the retrospective and anonymized nature of this study, the Research Ethics Committee waived the need to obtain informed consent from the study participants. The FDMA provided permission to use anonymized data from their database.

Results

Among 625,068 patients with OHCA registered from 2013 to 2017, a total of 245,759 patients suffered cardiac arrest with non-cardiac cause (Fig. 1). Of these, 1,449 adult patients had initial shockable heart rhythm and received witnessed arrest bystander CPR. After excluding 396 patients, 1,053 were eligible for this study. Of them, 57 (5.4%) were included in the bystander AED shock group and 996 (94.6%) in the EMS shock group.

The characteristics of the study population are summarized in Table 1. The most prevalent causes of cardiac arrest were others (43.5%), followed by respiratory disease (19.7%), and cerebrovascular disease (16.0%). There were no significant differences between the bystander AED shock group and EMS shock group with respect to age [70 (56–79) vs 72 (57–82) years, p = 0.27] or sex distribution [proportion of males: 41 (71.9%) vs 654 (65.7%), p = 0.33, respectively]. Patients in the bystander AED shock group received higher number of defibrillations by EMS personnel than those in the EMS shock group (p = 0.03). The time from witnessed arrest to first defibrillation by EMS did not differ between the bystander AED shock group and EMS shock group [13 (11–17) vs 13 (9–15) min, p = 0.49]. The time from witnessed arrest to initiation of bystander CPR [0 (0–4) vs 2 (0–4) min, p = 0.15], time from witnessed arrest to EMS contact [11 (9–15) vs 11 (9–13) min, p = 0.28], and time from witnessed arrest to hospital arrival [33 (26–37) vs 33 (28–42) min, p = 0.54] also did not differ between the two groups.

In the overall cohort, survival rate and rate of favorable neurological outcome at one month after cardiac arrest were 20.3% and 11.2%, respectively. There were no statistically significant difference in rates of one-month survival or favorable neurological outcome at one month between groups [16 (28.1%) vs 198 (19.9%), p = 0.14 and 9 (15.8%) vs 109 (10.9%), p = 0.26, respectively; Table 2].

Table 3 shows the unadjusted and adjusted association between the bystander AED shock before EMS shock and outcomes at 1 month after cardiac arrest. Logistic regression analysis revealed that bystander AED shock before EMS shock was not associated with survival [OR (95% CI): 1.57 (0.80–3.09), p = 0.19] or favorable neurological outcome [OR (95% CI): 1.63 (0.70–3.77), p = 0.25].

Discussion

This study assessed the impact of defibrillation with AED by bystander before defibrillation by EMS personnel on the outcomes of OHCA of presumed non-cardiac cause using the all-Japan OHCA registry. Only 5.4% patients received early defibrillation. We observed no association between defibrillation with AED by bystander before defibrillation by EMS personnel and favorable outcomes in OHCA of presumed non-cardiac cause. Our findings suggest the need to focus on the importance of early administration of cause-specific treatment for OHCA patients with non-cardiac cause.

We did not find any difference in the favorable outcomes of defibrillation with AEDs by bystander before defibrillation by EMS personnel in OHCA of presumed non-cardiac cause. The low contribution of defibrillation by bystander in OHCA of presumed non-cardiac cause might be explained by the physiological process of cardiac arrest. In patients with non-cardiac causes, systemic hypoxia or hypoperfusion are often the final events leading to cardiac arrest. In contrast, cardiac arrest due to cardiac causes is primarily caused by electrical change. According to the three-phase model, cardiac arrest can be divided physiologically into the electrical, circulatory, and metabolic phases,[19] and immediate defibrillation is most effective in the electrical phase.[20,19] Owing to the fact that shockable OHCA due to a non-cardiac etiology is the final pathophysiological state of circulatory and

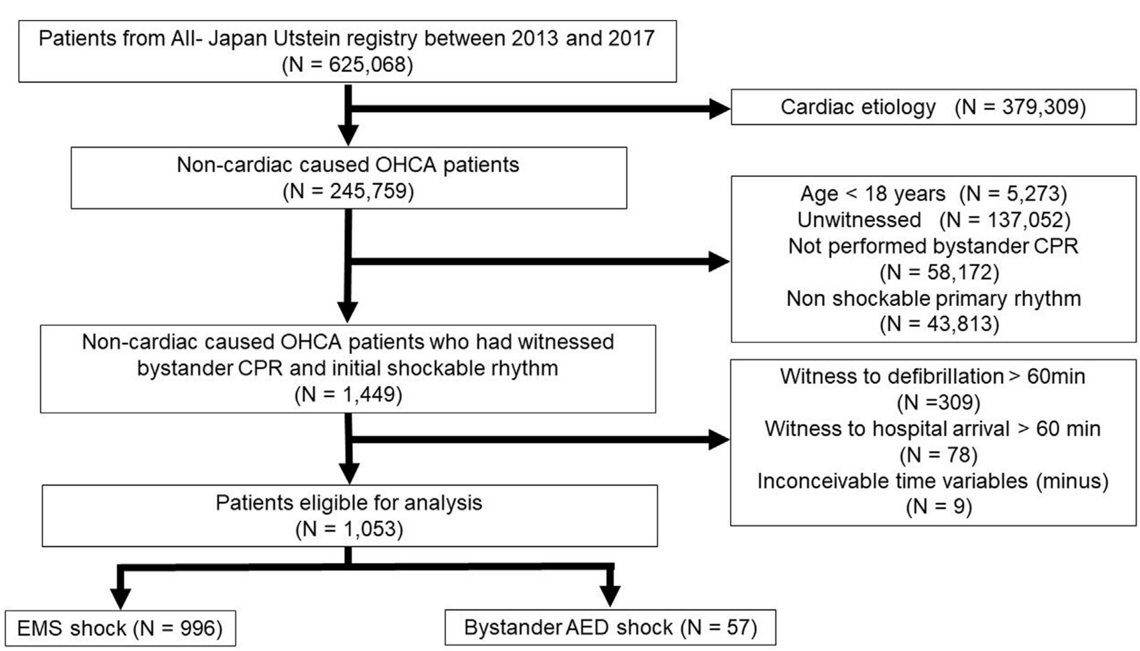

Fig. 1 – Flowchart of enrollment of study participants. OHCA: out-of-hospital cardiac arrest, CPR: cardiopulmonary resuscitation, EMS: emergency medical service.

Table 1 – Characteristics of patients with OHCA due to non-cardiac cause who had witnessed bystander CPR and initial shockable rhythm.

		EMS shock N = 996 (94.6)	Bystander AED shock N = 57 (5.4)	*P* value
Age (year)		72 (57–82)	70 (56–79)	0.27
Sex (male)		654 (65.7)	41 (71.9)	0.33
Initial heart rhythm	Ventricular fibrillation	970 (97.4)	55 (96.5)	0.68
	Pulseless ventricular tachycardia	26 (2.6)	2 (3.5)	
Type of non-cardiac cause	Cerebrovascular diseases	162 (16.3)	6 (10.5)	0.44
	Respiratory diseases	197 (19.8)	10 (17.5)	
	Malignancy	78 (7.8)	3 (5.3)	
	External factors	70 (7.0)	3 (5.3)	
	Toxication	6 (0.6)	0	
	Drowning	25 (2.5)	2 (3.5)	
	Traffic accident	22 (2.2)	2 (3.5)	
	Hypothermia	6 (0.6)	0	
	Anaphylaxis	2 (0.2)	1 (1.8)	
	Others	428 (43.0)	30 (52.6)	
Witness to first defibrillation by EMS time (min)		13 (9–15)	13 (11–17)	0.49
Number of defibrillations by EMS	1	522 (52.4)	21 (36.8)	0.03
	2	197 (19.8)	11 (19.3)	
	≥3	277 (27.8)	25 (43.9)	
Airway protective device use		390 (46.2)	20 (38.5)	0.28
Adrenaline use		345 (40.4)	23 (43.4)	0.66
Witness to bystander CPR time (min)		2 (0–4)	0 (0–4)	0.15
Witness to EMS contact time (min)		11 (9–13)	11 (9–15)	0.28
Witness to hospital arrival time (min)		33 (28–42)	33 (26–37)	0.54

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Chi-squared test.

OHCA: out-of-hospital cardiac arrest, AED: Automated External Defibrillator, CPR: cardiopulmonary resuscitation, EMS: emergency medical service, Missing: Witness to bystander CPR = 20, Airway protective device use = 157, Adrenaline use = 145.

Table 2 – Outcomes of OHCA due to non-cardiac cause in patients who had witnessed bystander CPR and initial shockable rhythm.

		EMS shock	Bystander AED shock	*P* value
		N = 996 (94.6)	N = 57 (5.4)	
Outcomes at one month	Survival	198 (19.9)	16 (28.1)	0.14
	Favorable neurological outcome (CPC = 1 or 2)	109 (10.9)	9 (15.8)	0.26

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Chi-squared test.

AED: Automated External Defibrillator, OHCA: out-of-hospital cardiac arrest, CPR: cardiopulmonary resuscitation, CPC: Cerebral Performance Category, EMS: emergency medical service.

Table 3 – Association between Bystander AED shock and outcomes at one month after cardiac arrest.

		Survival			Favorable neurological outcome		
		OR	95% CI		OR	95% CI	
Bystander AED shock (vs EMS shock)	Unadjusted	1.57	0.86	2.86	1.52	0.73	3.20
	Adjusted	1.57	0.80	3.09	1.63	0.70	3.77

N = 893 in logistic regression model.

Adjusted: age, sex, number of defibrillations, adrenaline use, witness to bystander CPR time, Witness to first defibrillation by EMS time, witness to EMS contact time, and witness to arrival hospital time.

AED: Automated External Defibrillator, OR: odds ratio, CI: confidential interval, EMS: emergency medical service, CPR: cardiopulmonary rescue.

metabolic disturbances, the effectiveness of earlier defibrillation by bystander before defibrillation by EMS personnel may be insufficient to improve the outcomes. Alternatively, the lack of observed association between defibrillation by bystander before by EMS personnel and outcomes in this study may simply be attributable to the small number of patients. Generally, a small proportion of OHCA patients have both witnessed arrest and initial shockable rhythms,[1,16] and this number may be even smaller for patients with non-cardiac cause. Further study with a larger sample size is warranted to verify the effect of defibrillation by bystander before defibrillation by EMS personnel on outcomes in OHCA with non-cardiac cause.

In our study, the proportion of cases in whom defibrillation with AEDs was performed by lay-person was low (5.4%), which was comparable with that reported from other countries. The proportion of defibrillation by lay-person varies widely among countries; 2.4% in England in 2014,[22] 1.6–3.1% in Canada between 2006–2013,[23] and 18.8% in the United States and Canada between 2011–2015.[7] These differences may be attributable to differences with respect to the study population, study design, and reference time-period.

In this study, favorable neurological outcome was observed in only about one-tenth of patients (118/1,053) with OHCA of presumed non-cardiac cause, who also had a shockable rhythm. In previous studies of cardiac arrest with non-cardiac cause, the initial heart rhythm mostly included asystole or PEA, which are believed to be associated with poor prognosis.[11–13] We included only OHCA patients with both witnessed arrest bystander CPR and initial shockable rhythm, who were considered to have the best chance of better outcomes. Nevertheless, the outcomes were not good enough.

Our study may not change practical strategy for resuscitation as bystanders would not be able to determine the probable cardiac cause and whether defibrillation is relevant. In addition, the number of shockable OHCA of presumed non-cardiac cause in this study is too small to show a significant difference between the study groups. As a result, it was very rare among patients with OHCA of 1,053/245,759 (0.4%). Nevertheless, we believe that this study is important as a basis for future research as it demonstrates the characteristics and outcomes of shockable OHCA of presumed non-cardiac cause, which previously received little attention. Although the strategy for resuscitation may not change, our study suggests that it is better to focus on the importance of specific treatment to address the underlying non-cardiac cause of cardiac arrest in these patients.

Limitations

Some limitations of our study should be acknowledged. First, the actual time from witnessed arrest to AED defibrillation by bystander was unknown. Few patients may have had longer time from collapse to AED use than from collapse to EMS defibrillation. This may have resulted in the underestimation of the association between defibrillation by bystander and outcomes. Whether bystander could deliver defibrillation before EMS arrival depended on where the cardiac arrest occurred or where the AED was installed. Although early defibrillation is necessary to achieve favorable outcomes, our data of 5.4% bystander AED shock might exhibited the limited availability of AED. Second, the quality of bystander CPR was not known. Differences in the quality of CPR in the two groups may have affected the results. Third, treatment after hospital arrival were not recorded, which may have affected the outcomes. However, OHCA patient included in this study were more likely to have been transported to national-certified emergency centers because they had both witnessed arrest and initial shockable rhythm and were expected to have the best prognosis in OHCA populations. Therefore, we believe that most patients received appropriate treatment.

Conclusions

The current study based on the Japanese national OHCA registry did not indicate that defibrillation with AEDs by bystander before defibrillation by EMS personnel was associated with favorable outcomes in OHCA patients of presumed non-cardiac cause.

Declaration of interest

The authors declare that they have no competing interests.

Acknowledgements

There is no funding. The authors would like to thank Enago (www.enago.jp) for the English language review.

Author details

[a]Department of Emergency and Critical Care Medicine, Tsukuba Memorial Hospital, Tsukuba, Japan [b]Department of General Medicine, Juntendo University Faculty of Medicine, Tokyo, Japan[c]Health Services Research and Development Center, University of Tsukuba, Tsukuba, Japan

REFERENCES

[1]. Drennan IR, Lin S, Thorpe KE, Morrison LJ. The effect of time to defibrillation and targeted temperature management on functional survival after out-of-hospital cardiac arrest. Resuscitation 2014;85:1623–8.

[2]. Dyson K, Brown SP, May S, et al. International variation in survival after out-of-hospital cardiac arrest: a validation study of the Utstein template. Resuscitation 2019;138:168–81.

[3]. Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013;310:1377.

[4]. Girotra S, Van Diepen S, Nallamothu BK, et al. Regional variation in out-of-hospital cardiac arrest survival in the United States. Circulation 2016;133:2159–68.

[5]. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med 1993;22:1652–8.

[6]. Blom MT, Beesems SG, Homma PCM, et al. Improved survival after out-of-hospital cardiac arrest and use of automated external defibrillators. Circulation 2014;130:1868–75.

[7]. Pollack RA, Brown SP, Rea T, et al. Impact of bystander automated external defibrillator use on survival and functional outcomes in shockable observed public cardiac arrests. Circulation 2018;137:2104–13.

[8]. Kitamura T, Kiyohara K, Sakai T, et al. Public-access defibrillation and out-of-hospital cardiac arrest in Japan. N Engl J Med 2016;375:1649–59.

[9]. Malta Hansen C, Kragholm K, Pearson DA, et al. Association of bystander and first-responder intervention with survival after out-of-hospital cardiac arrest in North Carolina, 2010–2013. JAMA 2015;314:255.

[10]. Kuisma M, Alaspaa A. Out-of-hospital cardiac arrests of non-cardiac origin: Epidemiology and outcome. Eur Heart J 1997;18:1122–8.

[11]. Engdahl J, Bång A, Karlson BW, Lindqvist J, Herlitz J. Characteristics and outcome among patients suffering from out of hospital cardiac arrest of non-cardiac aetiology. Resuscitation 2003;57:33–41.
[12]. Orban JC, Truc M, Kerever S, et al. Comparison of presumed cardiac and respiratory causes of out-of-hospital cardiac arrest. Resuscitation 2018;129:24–8.
[13]. Kitamura T, Kiyohara K, Sakai T, et al. Epidemiology and outcome of adult out-of-hospital cardiac arrest of non-cardiac origin in Osaka: a population-based study. BMJ Open 2014;4:e006462.
[14]. Committee. JRCCG. 2020 Japanese guidelines for emergency care and cardiopulmonary resuscitation. Tokyo: Igaku Shoin; 2021 (in Japanese).
[15]. Funada A, Goto Y, Tada H, et al. Age-specific differences in prognostic significance of rhythm conversion from initial non-shockable to shockable rhythm and subsequent shock delivery in out-of-hospital cardiac arrest. Resuscitation 2016;108:61–7.
[16]. Iwami T, Kawamura T, Hiraide A, et al. Effectiveness of bystander-initiated cardiac-only resuscitation for patients with out-of-hospital cardiac arrest. Circulation 2007;116:2900–7.
[17]. Weisfeldt ML, Becker LB. Resuscitation after cardiac arrest. JAMA. 2002;288:3035.
[18]. Vilke GM, Chan TC, Dunford JV, et al. The three-phase model of cardiac arrest as applied to ventricular fibrillation in a large, urban emergency medical services system. Resuscitation 2005;64:341–6.
[19]. Campbell RL, Hess EP, Atkinson EJ, White RD. Assessment of a three-phase model of out-of-hospital cardiac arrest in patients with ventricular fibrillation. Resuscitation 2007;73:229–35.
[20]. Hawkes C, Booth S, Ji C, et al. Epidemiology and outcomes from out-of-hospital cardiac arrests in England. Resuscitation 2017;110:133–40.
[21]. Buick JE, Drennan IR, Scales DC, et al. Improving temporal trends in survival and neurological outcomes after out-of-hospital cardiac arrest. Circ Cardiovasc Qual Outcomes 2018;11:e003561.