


# Survival to intensive care unit discharge among in-hospital cardiac arrest patients by applying audiovisual feedback device

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## Abstract

**Aims** Survival rates after in-hospital cardiac arrest remain very low. Although there is evidence that the use of audiovisual feedback devices can improve compression components, there are no data on patient survival. Therefore, we conducted this study to analyse the survival rate of patients with in-hospital cardiac arrest after discharge from the intensive care unit.

**Methods and results** This study was a secondary analysis of a prospective, randomized, controlled, parallel study of patients who received either standard manual chest compression or a real-time feedback device. Parametric and semi-parametric models were fitted to the data. Different survival time of length of stay was investigated by univariate and multiple analyses. Pearson's correlation between length of stay and hospital length of stay was obtained. A total of 900 patients with a mean survival time of 35 days were included. Intervention was associated with a higher length of stay. Relative time was significant in adjusted fitted log-normal regression for intervention group, female gender, and cardiopulmonary resuscitation in the night shift. A positive correlation between length of stay and hospital length of stay was found.

**Conclusions** Implementation of feedback device improved survival and length of stay. Cardiopulmonary resuscitation performance during the night shift decreased the survival time, which could be due to the inexperienced staff available outside working hours.

**Keywords** Survival; In-hospital cardiac arrest; Cardio First Angel™; ICU length of stay

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## Introduction

In-hospital cardiac arrest (IHCA) is associated with considerable morbidity and mortality. Cardiac arrest survival rate is still low despite cardiopulmonary resuscitation (CPR). During CPR, chest compression quality is the key for patient survival.<sup>1,2</sup> Various devices have been developed to improve the consistency and quality of chest compressions.<sup>3–6</sup> Some of these devices are combined with feedback technology to help guide

or inform rescuers of CPR. The complexity of CPR audiovisual feedback (AVF) devices ranges from a simple metronome to more complex metronome, which produces regular audible rhythms to help rescuers keep up. They measure CPR performance in real time and provide audiovisual information to guide rescuers to reach target depth and rate.<sup>7,8</sup> Several clinical and simulation studies have reported improved quality of compression components using AVF devices.<sup>9–15</sup> Furthermore, both the American Heart Association and the

International Liaison Committee on Resuscitation have issued cautious recommendations to support the use of AVF equipment.<sup>16–18</sup>

The AVF devices can be categorized as devices related or unrelated to automated external defibrillators (AEDs).<sup>19,20</sup> The non-AED devices are small, lightweight, portable devices that are positioned between the patient and rescuer. One of the devices in this category is Cardio First Angel™ (CFA; INOTECH, Nubberg, Germany), non-AED and an active compression–passive decompression feedback system, which was designed for use by both laypersons and healthcare professionals.<sup>21</sup> CFA is positioned on the patient’s chest where the rescuer’s hands would normally be positioned during manual CPR, and compressions are performed on the device.

The use of feedback devices to optimize CPR quality has been suggested in many previous studies, but it has not been shown to be associated with overall survival, so far.<sup>22–25</sup> Determining which resuscitation practices distinguish hospitals with high survival rates for IHCA remains a critical next step to advancing care in these high-risk patients.<sup>26</sup> Therefore, we conducted this trial study to determine whether the use of CFA compression feedback device improves rates of

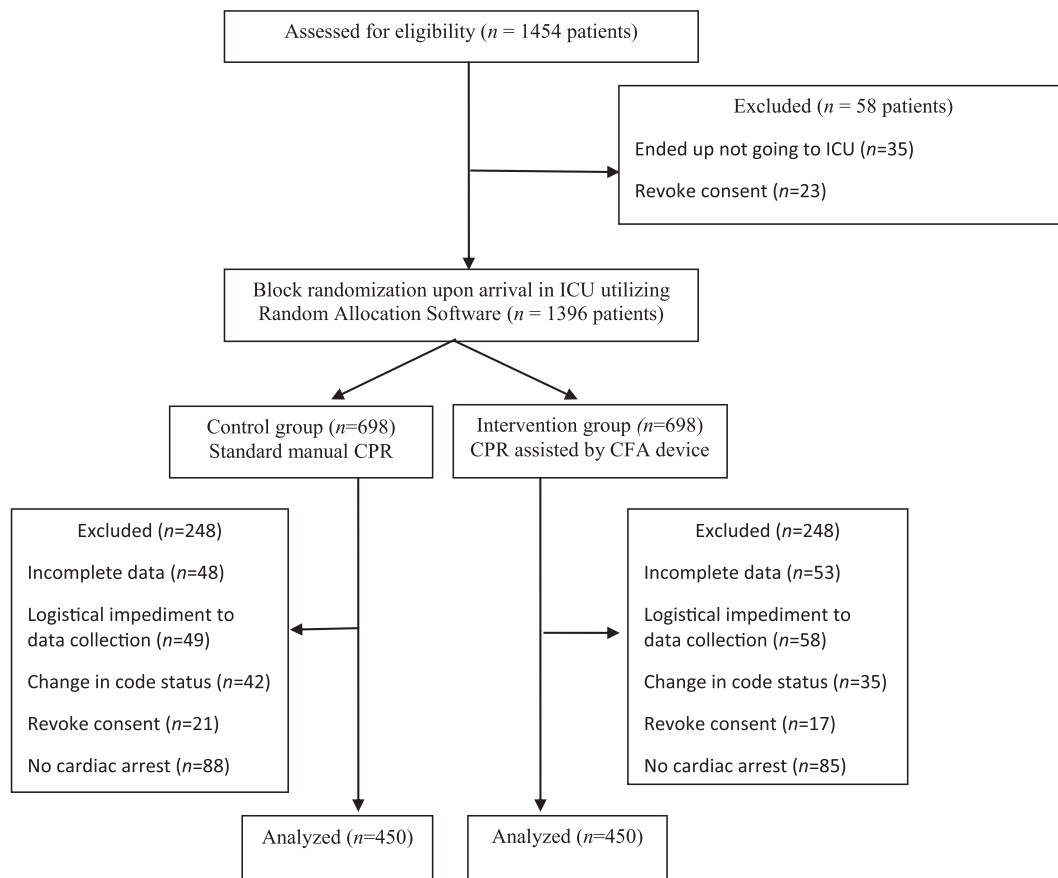
survival in intensive care unit (ICU) and hospital discharge for patients with IHCA.

## Methods

### Study design and settings

This study was a secondary analysis of a clinical trial. Its primary aim (i.e. sustained return of spontaneous circulation) has been achieved.<sup>21</sup> We sought to test a secondary objective (i.e. survival to ICU and hospital discharge) in the current study. The prospective, randomized, controlled, parallel study was conducted in Iran from 1 January 2015 to 15 September 2015. Study patients underwent resuscitation for the IHCA in medically and surgically mixed ICUs from eight academic higher care hospitals. All sections of the study illustrated in *Figure 1* are according to the Consolidated Standards of Reporting Trials statement.<sup>27</sup> The trial was registered at clinicaltrials.gov (Identifier NCT02845011). In the protocol, crossover design was not allowed.

**Figure 1** Flow chart of patient enrolment. CFA, Cardio First Angel™; CPR, cardiopulmonary resuscitation; ICU, intensive care unit.



## Randomization and blinding

Block randomization was performed in four-person groups using a random number list generated by random allocation software © (Informer Technologies, Inc., Madrid, Spain; *Figure 1*). The numbers were placed in successive containers to be kept in a safe place until allocation. The allocation sequences and participant's enrolment were performed separately by different researchers to ensure blindness. The third researcher was responsible for follow-up and assessment of patients. Emergency department enrolment and randomization were only selected from patients admitted to ICU. Hence, patients who agreed to enrol in the study had received cardiac arrest treatment during the intensive care unit stay. A container was located at the foot of the bed, containing either a CFA (intervention) or a sham (control) device. As soon as the resuscitation began, the container would be opened and the providers would perform the resuscitation accordingly. After the trial, no significant changes were made in the methods and the study ended after receiving the required sample size. In addition, patients and data analyser were blinded to randomization. However, healthcare providers were not blind at the time of resuscitation because it was considered unethical to use a sham device.

## Inclusion and exclusion criteria

Inclusion criteria in this study, in addition to admission to the ICU of emergency department, were as follows: (i) age over 18 years, (ii) patients with cardiac arrest, (iii) resuscitation status (full code), and (iv) informed consent. The latter was obtained, at admission, by the patient's legal guardian or healthcare proxy if the patient did not have decision-making capacity. Exclusion criteria were as follows: (i) cardiac arrest prior to enrolment at the emergency department or cardiac arrest out of hospital, (ii) code status except for full code, (iii) cancelled consent, and (iv) missing or incomplete data due to any logical obstacles during data collection and pregnancy.

## Participants and procedure

A total of 1396 patients (or legal guardian or an appropriate successor who was able to make consent decisions) signed consent at randomization. Decisions to cease resuscitation efforts were made by the team leader in accordance with the European Resuscitation Council and American Heart Association guidelines. These decisions comprised (i) asystole for more than 20 min in the absence of any reversible cause [e.g. cardiac tamponade, tension pneumothorax, distributive shock (anaphylaxis), hypothermia at the time of arrest, and chemical intoxication/overdose (e.g. opiate)], (ii)

resuscitation longer than 30 min without ventricular fibrillation or ventricular tachycardia any time (initial or subsequent rhythm), (iii) injury incompatible with life, and (iv) co-morbidities' severity.<sup>18,28</sup> The decision for ceasing resuscitation was made for those patients with ventricular fibrillation or ventricular tachycardia without continuous pulse and unresponsive to CPR, defibrillation, and medications. These decisions were also made on the basis of clinical parameters such as evident vs. non-evident arrest, time to start CPR, co-morbidities, and pre-arrest state.

## Intervention

All arrests that occurred in ICU were categorized as evidenced and simultaneously monitored. One intensivist, three to five ICU nurses, and a respiratory specialist consisted the resuscitation team. The resuscitation was performed based on standard guidelines as follows: (i) chest compression carried out by skilled ICU nurses, (ii) defibrillation (either conventional method or automated), (iii) prescribed medications (e.g. epinephrine, vasopressin, atropine, amiodarone, sodium bicarbonate, calcium chloride, and magnesium sulfate), and (iv) ventilation in the presence or absence of endotracheal intubation. The defibrillation technique was the same as the standard baseline procedure for all participants. All ICU nurses received standard CPR training in accordance with published guidelines and were trained to use CFA device at approved study centres.<sup>29,30</sup> Patients in the control group received CPR according to the published guidelines. Conversely, the CFA feedback device was applied for chest compressions in intervention group. Invasive haemodynamic measurements were beyond the scope of this study.

## Cardio First Angel device

Cardio First Angel is a lightweight three-component handheld device. The rescuer side has a red palm-sized press button along with a pictogram to display the proper usage of the device (*Figure 2*). The patient side has a liquid absorbable polyurethane foam. The central unit consists of a spring-loaded plastic base. Once the pressure force reaches  $400 \pm 30$  N, an audible 'click' notifies the rescuer to stop the compression. Similarly, releasing the compression is followed by another click that indicates compression resumption.<sup>7</sup>

## Data collection

The secondary outcomes of the trial were survival to ICU and hospital discharge. Survival time was defined as the ICU length of stay (days), and ICU survival was defined as a binary variable (alive and dead) to indicate the survival status of the patient. Collected demographic data included treatment

**Figure 2** Pictogram for displaying the proper use of the device.



received, sex, age, intubation prior to CPR initiation, intubation during CPR, multi-organ dysfunction (respiratory, haematology, liver, cardiovascular, central nervous system, and renal), CPR shift, CPR duration, initial rhythm, first shock, biphasic shock, diagnosis, underlying osteoporosis, and frequency of conducted CPR. There were no important changes to methods after trial commencement. Information for invasive arterial monitoring and capnography wave was not reported as these procedures are not commonly available for patients.

### Statistical analyses and modelling

Final sample size assuming an alpha of 0.05, a power of 0.9, and 10% attrition, based on survival and morbidity data, was 450 subjects per group. Calculations were performed using STATA<sup>®</sup> 14 (StataCorp LLC, College Station, TX, USA). Variables were individually entered into the crude Cox model, and the significant ones were entered into the multiple Cox proportional hazard model. Proportional hazard assumption was evaluated by Schoenfeld residuals. Parametric models including Weibull, log-normal, and log-logistic were fitted to the data; the Weibull model could be expressed by both hazard ratio and relative survival time, while the log-logistic and

log-normal model could only be expressed by relative survival time, that is, time ratio (TR). The fitted models were subsequently compared using Akaike information criterion (AIC) in which a lower AIC indicates a better fit. Besides, the frailty component with gamma distribution was added to the best-fitted model to account for variability unaccounted by the model. Finally, the correlation between ICU length of stay and hospital length of stay was estimated using Spearman's rho correlation coefficient.

## Results

### Participants of the study

Of the 1454 subjects assessed for eligibility, 58 pre-randomization and 496 post-randomization (control and intervention groups) were excluded (554 subjects were excluded overall). Thus, data were analysed in 900 patients during ICU stay (*Figure 1*). The high number of ICU patients was because most of them had internal diseases or serious surgery and so were transferred to the general ICU (about half of the patients had multi-organ dysfunction syndrome, which had significantly lower sustained return of spontaneous circulation). The mean and median of staying in ICU were 34.70 (SE = 0.82) and 30 (SE = 0.62) days, respectively. Descriptive statistic of study participants is shown in *Table 1*.

### Findings of crude Cox model

The crude models of Cox and log-normal were fitted (*Table 2*). In the crude Cox model, the intervention group had nearly 50% lower hazard compared with the control group [hazard ratio = 0.51 (0.42, 0.61),  $P < 001$ ]. Women had 32% worsen survival time compared with men [hazard ratio = 1.32 (1.10, 1.59),  $P < 001$ ]. However, the results of the log-normal model show that the patients who received intervention had 32% better survival time compared with the ones who received control [TR = 1.32 (1.23, 1.42),  $P < 001$ ] and women had 13% lower survival time compared with men [TR = 0.87 (0.80, 0.92),  $P < 001$ ]. The time of the day in which the CPR was performed was also significant in the crude log-normal model. Patients who underwent CPR during night shift had 14% worse survival time compared with the ones who received CPR during the morning shift [TR = 0.86 (0.76, 0.98),  $P = 0.02$ ]. The duration of CPR longer than 43 min reduced the survival time by 10% [TR = 0.90 (0.84, 0.97),  $P < 0.01$ ]. These significant factors were entered into the multiple Cox and log-normal model. The result of multiple Cox regression indicated a significant value for intervention ( $P$ -value  $< 0.01$ ) and sex ( $P$ -value  $< 0.01$ ); however, the proportional hazard assumption was not satisfied for these two variables.

**Table 1** Summary of survival time of ICU length of stay (days)

Variable		Number of patients	Number of mortality	Mean survival time (SE)
Treatment	Intervention	450	181	39.57 (1.37)
	Control	450	299	30.34 (0.94)
Sex	Female	546	293	33.61 (1.14)
	Male	354	187	36.58 (1.16)
Intubated prior to CPR event	Yes	368	195	35.16 (1.28)
	No	532	285	34.47 (1.06)
Intubated during CPR	Yes	70	39	32.45 (2.06)
	No	830	441	34.92 (0.87)
Multi-organ dysfunction	Yes	438	245	34.64 (1.17)
	No	462	235	34.24 (1.08)
CPR shift	Night	103	56	32.59 (2.86)
	Evening	310	172	33.80 (1.35)
	Noon	315	161	36.15 (1.47)
	Morning	172	91	35.50 (1.72)
Rhythm	Asystole	368	205	34.63 (1.33)
	VT	71	32	34.32 (3.29)
	VF	103	63	31.25 (1.46)
	Bradycardia	358	180	35.40 (1.28)
First shock	Yes	106	61	31.68 (1.83)
	No	794	419	35.12 (0.90)
Biphasic shock	0	484	266	34.46 (1.02)
	400	120	52	35.71 (2.12)
	600	155	85	35.39 (2.11)
	800	109	59	30.76 (2.47)
	1000	32	18	36.63 (3.69)
Age	≤55	456	238	34.04 (1.05)
	>55	444	242	35.04 (1.19)
CPR duration	≤43	450	239	35.87 (1.22)
	>43	450	241	33.04 (0.98)
Frequency of conducted CPR	1	422	238	34.50 (1.06)
	2	433	217	35.67 (1.42)
	3	45	25	30.35 (1.87)
Diagnosis	Trauma	41	21	35.47 (4.49)
	Neurological	169	84	37.51 (2.13)
	Renal	219	124	34.69 (1.7)
	Cancer	228	128	31.55 (1.05)
	Respiratory	198	93	33.04 (1.05)
Osteoporosis	Abdominal infection	45	30	32.03 (2.48)
	Yes	438	219	35.98 (1.33)
	No	462	261	33.49 (0.96)

CPR, cardiopulmonary resuscitation; ICU, intensive care unit; SE, standard error; VF, ventricular fibrillation; VT, ventricular tachycardia.

### Different parametric models

Different parametric models such as Cox, Weibull, log-logistic, log-normal, and log-normal with gamma frailty were compared using AIC. Among these models, log-normal distribution with gamma frailty and the lowest AIC showed the best fit. The results of the AIC comparison are shown in Supporting Information, *Table S3*. After fitting the log-normal model with gamma frailty, significant variables in the crude model including treatment, sex, CPR shift, and CPR duration were entered into the multiple models.

### Findings of multiple regression model

As illustrated in Supporting Information, *Table S4*, patients who received the intervention had 31% better survival time compared with the control group [TR = 1.31 (1.22, 1.40),  $P < .001$ ] (Supporting Information, *Figure S3*). Women

compared with men had a 13% worse survival time [TR = 0.87 (0.81, 0.93),  $P < .01$ ] (Supporting Information, *Figure S4*). In addition, CPR performed during night shift reduced the survival time by 15% [TR = 0.85 (0.75, 0.97),  $P = .01$ ] (Supporting Information, *Figure S5*).

### Correlation between hospital and intensive care unit length of stay

The descriptive statistics of the ICU length of stay and hospital length of stay are shown in Supporting Information, *Table S5*. The mean and median staying in hospital were 52.75 and 46 days, respectively. There was also a high positive correlation between these two variables ( $P < .001$ ). The results of survival analysis on length of stay for ICU and hospital were similar, so we only showed the ICU analysis in this study.

**Table 2** Results of crude regressions of ICU length of stay (days)

Variable		Crude Cox model		Crude log-normal model	
		Hazard ratio (95% CI)	P-value	Relative time (95% CI)	P-value
Treatment	Intervention	0.51 (0.42, 0.61)	<0.01*	1.32 (1.23, 1.42)	<0.01*
	Control	Ref		Ref	
Sex	Female	1.32 (1.10, 1.59)	<0.01*	0.87 (0.80, 0.92)	<0.01*
	Male	Ref		Ref	
Intubated prior to CPR event	Yes	0.98 (0.82, 1.18)		1.02 (0.95, 1.09)	0.64
	No	Ref		Ref	
Intubated during CPR	Yes	1.06 (0.77, 1.48)	0.69	0.99 (0.87, 1.13)	0.88
	No	Ref		Ref	
Multi-organ dysfunction	Yes	1.06 (0.89, 1.28)	0.46	0.97 (0.90, 1.04)	0.41
	No	Ref		Ref	
CPR shift	Night	1.34 (0.96, 1.88)	0.08	0.86 (0.76, 0.98)	0.02*
	Evening	1.15 (0.89, 1.48)	0.28	0.94 (0.85, 1.04)	0.25
	Noon	0.98 (0.76, 1.27)	0.88	0.99 (0.89, 1.09)	0.87
	Morning	Ref		Ref	
Rhythm	Asystole	1.15 (0.94, 1.41)	0.17	0.93 (0.86, 1.01)	0.08
	VT	1.06 (0.72, 1.55)	0.77	1.01 (0.88, 1.15)	0.95
	VF	1.23 (0.92, 1.64)	0.16	0.91 (0.81, 1.02)	0.09
	Bradycardia	Ref		Ref	
First shock	Yes	1.23 (0.94, 1.61)	0.14	0.96 (0.86, 1.06)	0.41
	No	Ref		Ref	
Age	≤55	Ref		Ref	
	>55	0.98 (0.82, 1.18)	0.85	0.99 (0.92, 1.06)	0.81
CPR duration	≤43	Ref		Ref	
	>43	1.13 (0.94, 1.35)	0.20	0.90 (0.84, 0.97)	<0.01*
Frequency of conducted CPR	1	Ref		Ref	
	2	0.99 (0.82, 1.19)	0.91	0.98 (0.91, 1.05)	0.58
	3	1.10 (0.73, 1.66)	0.65	0.96 (0.82, 1.13)	0.61
Diagnosis	Trauma	Ref		Ref	
	Neurological	0.84 (0.52, 1.36)	0.48	1.05 (0.87, 1.26)	0.61
	Renal	1.05 (0.66, 1.67)	0.84	0.95 (0.80, 1.14)	0.61
	Cancer	1.10 (0.69, 1.75)	0.68	1.01 (0.85, 1.22)	0.87
	Respiratory	0.89 (0.55, 1.44)	0.65	1.08 (0.89, 1.29)	0.46
	Abdominal infection	1.16 (0.66, 2.03)	0.60	0.99 (0.79, 1.24)	0.94
Osteoporosis	Yes	Ref		Ref	
	No	1.12 (0.93, 1.34)	0.23	0.99 (0.79, 1.24)	0.94

CI, confidence interval; CPR, cardiopulmonary resuscitation; ICU, intensive care unit; VF, ventricular fibrillation; VT, ventricular tachycardia.  
\*Significant at 0.05 level.

## Discussion

Improved survival after cardiac arrest occurs regardless of whether or not the initial cardiac arrest rhythm is responsive to defibrillation. This implies the potential role of other factors in improvement of survival such as early recognition of cardiac arrest, quality of acute resuscitation, use of feedback devices to optimize CPR quality, and post-resuscitation care.

Mean survival time of ICU length of stay in the study was 34.70 days, which is consistent with the study by Lipsett *et al.*<sup>31</sup> However, it is considerably higher than the mean ICU length of stay in several studies.<sup>32–36</sup> The differences in survival time among studies might be related to several factors such as differences in definition of survival, populations, or the study settings.<sup>37</sup>

In the current study, relative time was significant in adjusted fitted log-normal regression for intervention, female gender, and CPR in night shift. According to the results, survival time in the intervention group was 31% better than the control group, female patients had 13% shorter survival time than men, and CPR performed during the night shift

reduced survival time by 15%. Based on a retrospective study conducted by Böhmer *et al.*,<sup>36</sup> conservative treatment was significantly associated with improvement in ICU length of stay. Inconsistent with our results, the results of Böhmer *et al.*<sup>36</sup> study showed that women had a better survival rate. In addition, previous studies have shown that CPR carried out during the day yielded more favourable outcome, which was consistent with our results.<sup>38–40</sup> However, in the studies by Goharani *et al.*<sup>41</sup> and Vahedian-Azimi *et al.*,<sup>21</sup> CPR performance did not have any significant association with the survival.

In line with our results, a study by Syue *et al.*<sup>42</sup> reported that the chance of survival of patients with IHCA was lower during the night shift than the morning or evening shift. However, Goharani *et al.*<sup>41</sup> study employed multiple logistic regression and did not find any significant association between the CPR performance on any time of the day and survival. It should be noted that CPR delivered during working hours (8 a.m. to 4 p.m.) usually results in more survivors than those performed outside working hours (4 p.m. to 8 a.m.). Although the ICU has highly skilled staff and fully

equipped at all times, less experienced and less staff are available outside working hours. Moreover, tiredness of the remaining staff can contribute to poor outcome.<sup>43</sup>

The issue was that there was uncertainty about improving survival using the feedback devices. By the primary outcome of return of spontaneous circulation in the Goharani *et al.*<sup>41</sup> study and its secondary analysis of survival to ICU discharge (which was expanded in this study), we showed the desired quality of non-AED free-standing AVF devices if it complied with the revised guidelines. Also, in the meta-analysis study of Miller *et al.*,<sup>22</sup> the improvement of survival to ICU discharge was concluded by the AVF devices. It is worth noting that among the numerous feedback devices, there were fewer published human randomized controlled trials.<sup>21,41,44</sup> Because of lack of sufficient data, our study will be the basis for the future.

### Limitations

The limitations of this study are as follows: (i) no record of primary cardiac conditions; (ii) not designed to follow neurological outcomes; (iii) not designed to record data on compression rate and depth, chest recoil, duration of interruptions, no flow time, or flow fraction; (iv) no report of invasive arterial surveillance and wave form capnography due to unavailable data; and (v) no report of post-resuscitation process. Inability to blind the clinical providers was a notable limitation of compression feedback device studies. It is possible to blind the subject, the investigator, and the data analyser, which was performed in this study. However, blinding the health provider required either (i) use of a sham device or (ii) hiding the device during compression pauses. Hence, applying a sham device was deemed to be unethical and hiding the device was impossible in practice. Besides, do-not-attempt-resuscitation law does not apply in the country where the study was conducted. However, only full-code patients were included in this study. Complex changes in compliance of chest wall as well as compressibility of the surface the patient is lying on (e.g. mattress) were stated as criticisms of the current non-AED compression feedback devices. Also, the non-uniformity of assessment for chest wall complications, which was partly due to limited funding, prevents the conclusions from expanding.

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## Conclusion

Globally, the high rate of cardiac arrest mortalities over these years may have been due to poor-quality CPR performance by medical professionals and lay providers. However, our analysis has demonstrated that the use of CFA non-AED device provides longer relative survival time among patients.

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## Conflict of interest

None declared.

## Funding

None.

## Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S3.** Kaplan–Meier survivor function for treatment.

**Figure S4.** Kaplan–Meier survivor function for sex.

**Figure S5.** Kaplan–Meier survivor function for CPR shift.

**Table S3.** Comparison between regression models for ICU length of stay (days).

**Table S4.** Fitted lognormal regression of ICU length of stay (days).

**Table S5.** Descriptive statistic of ICU length of stay and Hospital length of stay.

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