Influence of advanced life support response time on out-of-hospital cardiac arrest patient outcomes in Taipei

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Abstract

Background

The association between out-of-hospital cardiac arrest patient survival and advanced life support response time remained controversial. We aimed to test the hypothesis that for adult, non-traumatic, out-of-hospital cardiac arrest patients, a shorter advanced life support response time is associated with a better chance of survival. We analyzed Utstein-based registry data on adult, non-traumatic, out-of-hospital cardiac arrest patients in Taipei from 2011 to 2015.

Methods

Patients without complete data, witnessed by emergency medical technicians, or with response times of ≥ 15 minutes, were excluded. We used logistic regression with an exposure of advanced life support response time. Primary and secondary outcomes were survival to hospital discharge and favorable neurological outcomes (cerebral performance category ≤ 2), respectively. Subgroup analyses were based on presenting rhythms of out-of-hospital cardiac arrest, bystander cardiopulmonary resuscitation, and witness status.

Results

A total of 4,278 cases were included in the final analysis. The median advanced life support response time was 9 minutes. For every minute delayed in advanced life support response time, the chance of survival to hospital discharge would reduce by 7% and chance of favorable neurological outcome by 9%. Subgroup analysis showed that a longer advanced life...
support response time was negatively associated with the chance of survival to hospital discharge among out-of-hospital cardiac arrest patients with shockable rhythm and pulse electrical activity groups.

Conclusions
In non-traumatic, adult, out-of-hospital cardiac arrest patients in Taipei, a longer advanced life support response time was associated with declining odds of survival to hospital discharge and favorable neurologic outcomes, especially in patients presenting with shockable rhythm and pulse electrical activity.

Introduction
Out-of-hospital cardiac arrest (OHCA) is a major disease worldwide, with a high mortality rate. Taiwan has approximately 9,815 cases of OHCA annually, with a survival rate of approximately 9.8% [1]. Time is one of the most important prognostic factors, especially the emergency medical services (EMS) response time. The EMS response time, the period of time from the call to EMS arrival at the scene, is associated with the survival rate among OHCA patients [2]. Several recent reports showed that shorter EMS response times improve the survival rates and neurological outcomes in patients with OHCA [2–11].

The effect of advanced life support (ALS) treatments in prehospital settings remains controversial. Several studies reported that earlier ALS intervention is associated with increasing survival rate [12–16], while others revealed worsening or no benefit to survival [17–19]. Thus, the association between the survival of OHCA patients and ALS response time remains controversial and unclear. Grunau et al. and Kurz et al. [20, 21] demonstrated that early ALS arrival at the scene can reduce mortality, but Michelland et al. [22] showed no benefit to early ALS response time.

Regarding the EMS system in Taipei, previous studies showed that the intervention of ALS and the number of ALS personnel are associated with better outcomes in OHCA patients [11, 23–27]; however, the exact influence of ALS response time has not yet been examined. Thus, the objective of this study was to determine whether a shorter ALS response time was associated with an improved chance of survival in non-traumatic, adult, OHCA patients.

Methods
Study design and setting
We conducted a 5-year retrospective cohort study using prospectively collected Utstein-based registry data from the Taipei EMS to investigate the association between the response time of ALS care and OHCA patient outcomes. All methods were performed in accordance with the study protocol which was approved by the Institutional Review Board (IRB) of the National Taiwan University Hospital (201606007RIND). Informed consent was waived due to the anonymized database and retrospective nature of the study, which was also approved by IRB of the National Taiwan University Hospital. The preliminary version of the abstract had been published at the European Resuscitation Council annual conference 2019 in Slovenia before we develop it into a full-length article.
Data source

The Utstein-based OHCA registry system from the Taipei EMS was initially developed for OHCA quality control [28]. The registry system data comprised dispatch records, modes and timing of prehospital care, patient demographics, arrest characteristics (witness status, bystander Cardiopulmonary Resuscitation (CPR), initial rhythm, and cardiac monitor), records on automated external defibrillator (AED), prehospital ALS treatment, and patient outcomes (survival to hospital discharge and neurologic status at discharge) [25]. The rate of missing data ranged from 0% to 2.6%.

Taipei EMS system

Taipei City, a metropolitan area in Taiwan, Southeast Asia, covers 272 km$^2$, with 2.6 million registered residents. The majority of the population is Taiwanese. Taipei City has an EMS system based on the fire service with a two-tiered response team, including a basic life support (BLS) team and an ALS team. Taipei City has 45 prehospital BLS stations with 1,279 emergency medical technician (EMT) intermediate staff, who have completed at least 320 hours of training; and four ALS stations with 141 EMT paramedics, who have completed at least 1280 hours of training and need to conduct OHCA re-training every year [25]. The BLS team is capable of performing defibrillation and placing a laryngeal mask airway (LMA). One BLS station has two BLS ambulances, and each ambulance is usually teamed with two EMTs, sometimes three, depending on the available human resources at the time of dispatching [25]. The ALS team providers are authorized to perform endotracheal tube intubation and intravenous injections of resuscitation medications, such as adrenaline, atropine, and amiodarone, as per protocol [28]. One ALS station has three ALS ambulances, each usually teamed with two paramedics.

There is a single central dispatch center in Taipei to handle all incoming EMS calls; all dispatchers are required to complete 40 hours of training on priority dispatch. The BLS team is the universal response for all dispatch calls. For cases that meet the ALS dispatch criteria, such as out-of-hospital cardiac arrest, foreign body airway obstruction, major trauma, consciousness change and chest pain judged by dispatchers through the calls, additional ALS teams are dispatched to the scene together with BLS teams. For an ALS case that occurs in an area close to an ALS squad, the nearby ALS team is the first response team to dispatch, and an additional ALS team, as opposed to a BLS, will be activated if available [25].

Study population

We analyzed OHCA patients in Taipei from 1 January 2011 to 31 December 2015. The eligible patients were adults (aged ≥ 20 years) with non-traumatic OHCA who underwent resuscitation attempts by the ALS team. Patients without complete data, with OHCA witnessed by EMT, with traumatic OHCA, or a response time longer than 15 minutes were excluded. Patients were also excluded if they were not transported to the hospital due to obvious signs of death, such as rigor mortis, if the family requested a do-not-resuscitate (DNR), or if the patient had a pre-existing DNR. We then divided the study population (Any ALS) into two groups, ALS dispatched only (only ALS) and ALS and BLS dispatched (ALS+BLS). We did not differentiate the arrival sequence in the unit of ALS+BLS, because the time interval between both groups was close, and the BLS assessment might have been affected by the ALS team.

Definition of exposures

The key exposures in our study were ALS response time, defined as the interval from first EMS dispatch call to first ALS team arriving at the scene by the centralized time of dispatch. Other
characteristics included EMS response time, witnessed OHCA, bystander CPR, shockable rhythm, OHCA happening in public places, scene time, transporting to medical centers, injecting adrenaline prehospitaly, injecting other medications prehospitaly, such as atropine and amiodarone, and endotracheal tube intubation. EMS response time was defined as the period of time from to the call to EMS arrival at the scene (regardless of BLS or ALS team); shockable rhythm was defined as the heart rhythm showing pulseless ventricular tachycardia (pVT) or ventricular fibrillation (Vf) during resuscitation and scene time was defined as the portion of time between arrival of the ambulance on scene of the patient and when the ambulance departs the scene.

**Outcome measurement**

The primary outcome was survival to hospital discharge. The secondary outcome was favorable neurological outcome, defined as cerebral performance category (CPC) level 1 and 2 [29], which is a key endpoint for several prominent clinical trials [30, 31] and a core recommended outcome measure for cardiac arrest registries [32].

**Statistical analysis**

We used Excel (Microsoft, Redmond, WA, USA) to record data and SAS version 9.3 (SAS Institute, Cary, NC, USA) to analyze the data. The descriptive statistics for the population are presented as counts, percentages, or medians (interquartile range [IQR] Q1–Q3). We performed chi-squared or Fisher's exact tests to assess the associations between the categorical variables and outcomes. For continuous variables, we conducted non-parametric Mann–Whitney rank sum tests for analyses. All variables previously determined to be associated with the outcomes were included in the multivariable logistic regression analysis to prevent overfitting. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and two-tailed p-values < 0.05 were considered statistically significant.

We conducted a subgroup analysis using the new Utstein template, with methods suggested by the International Liaison Committee on Resuscitation (ILCOR) in 2014, to explore the effect of ALS response time among different subgroups of patients with OHCA. For this analysis, we stratified the data based on presenting rhythms of OHCA, including shockable rhythm (pVT/Vf), pulseless electrical activity (PEA), and asystole [33]. We also analyzed a subgroup of patients with witnessed OHCA and patients with bystander CPR. Known Utstein covariates, including age, sex, witnessed OHCA, bystander CPR, shockable rhythm, total EMT numbers, and EMS response time were adjusted. We further separated the ALS response time into categorical variables (< 8 minutes, 8–11 minutes, ≥ 11 minutes) by patient numbers to explore the cut-off value of the ALS response interval. A restricted cubic spline model was performed on the total study population and subgroup analysis to visualize the association between ALS response time and survival to hospital discharge.

**Results**

**Study population**

Of the 16,062 OHCA cases treated between 2010 and 2015, 7,571 cases were adult, non-trauma OHCA without EMT witness with resuscitation attempted and 4,278 cases with ALS dispatch were included in the final analysis. (Fig 1) The proportion of ALS dispatch cases were 56.5% (4278/7571). Patient characteristics are listed in Table 1. The median ALS response time was 9 minutes (IQR 7–12), the median response time of the first ambulance was 5 minutes (IQR 4–6), and the median scene time was 15 minutes (IQR 13–18). A total of 1366 (31.93%)
patients received an adrenaline injection, and 789 (18.44%) patients received endotracheal tube intubation. A total of 993 (23.21%) patients achieved a return of spontaneous circulation (ROSC), 287 (6.71%) survived to discharge, and 126 (2.95%) had a favorable clinical outcome (CPC ≤ 2) at discharge.

Outcomes

Table 2 shows the adjusted odds ratio (aOR) for survival to hospital discharge and favorable clinical outcomes in different groups based on ALS response time (per minute). For every minute of delayed ALS response time, the likelihood of survival to hospital discharge would reduce by 7% (aOR 0.93; 95% CI: 0.89–0.97) in all OHCA patients. Further, for every minute of delayed ALS response time, there was a reduction of 9% (aOR, 0.91; 95% CI: 0.85–0.97) chance of favorable neurologic outcome (CPC ≤ 2) at discharge. Univariate analysis of each group in Table 2 were showed in S1 and S2 Tables. In the subgroup analysis, the chance of
survival to hospital discharge decreased by 9% (aOR 0.91; 95% CI: 0.85–0.97) in the shockable rhythm (pVT/Vf) group, decreased by 9% (aOR 0.91; 95% CI: 0.85–0.98) in the PEA rhythm group, and had no significant benefit in the asystole rhythm group. The chance of a favorable neurological outcome at discharge decreased by 9% (aOR 0.91; 95% CI: 0.85–0.97) every minute in general ALS resuscitation, by 11% (aOR 0.89; 95% CI: 0.81–0.96) in shockable rhythm, and 12% (aOR 0.88; 95% CI: 0.78–0.996) in PEA. Similarly, there were no significant benefits in the asystole rhythm group.

Table 3 further demonstrates the aOR of survival to hospital discharge and favorable neurological outcome after separating ALS response time to tertiles. We found that compared to the group with ALS response time of less than 8 minutes, in the group with ALS response time over 11 minutes every minute of delayed ALS response time would decrease by 40% (aOR 0.6; 95% CI: 0.43–0.84) the chance of survival to hospital discharge, as well as favorable neurologic outcome (aOR 0.59; 95% CI: 0.35–0.97). We found a similar result in the group of witnessed OHCA patients and the group receiving bystander CPR. Favorable neurological outcome was not statistically significant in the bystander CPR group.

The restricted cubic spline curve in Fig 2 demonstrates the estimated trend of decrease in the rate of survival to hospital discharge as ALS response time increases, which has a sharper step-wise decline in the chance of survival with increasing time intervals. The decline stabilized at approximately 8 minutes. Fig 3 further demonstrates the estimated results of the subgroup divided by initial rhythm (pVT/Vf, PEA, asystole). The group of shockable rhythm and PEA also demonstrates a trend of decline in the chance of survival with increasing ALS response time intervals.
Discussion

In this large observational study in Taipei, we found that every minute of delay in ALS response time was associated with a 7% reduction in survival to hospital discharge and a 9% reduction in favorable neurological outcome in adult, non-traumatic, OHCA patients. A swift response by ALS not only benefited all OHCA patients, but also significantly benefited the subgroups of patients initially presenting shockable rhythms or PEA. An ALS response time of less than 8 minutes was associated with better outcomes in OHCA patients, while over 11 minutes was associated with a diminished chance of survival. We previously announced the preliminary results of this study [11], which was also consistent to our final results.

Our findings are similar to those of Grunau et al. [20], with new information. Their study demonstrates that the rate of survival to hospital discharge decreases by 3% for each minute of delayed ALS response time (aOR 0.97, 95% CI: 0.96–0.98). The results are consistent with ours, except for different decrease rates, which could be attributed to a higher proportion of patients with shockable rhythm and a higher proportion of bystander CPR rates. We further observed a benefit of early ALS arrival in the subgroup of patients with PEA. In our subgroup analysis, every minute of delayed ALS response time decreased the survival to hospital discharge by 9% (aOR 0.91, 95% CI: 0.85–0.98) in the PEA group. The deteriorating rate was almost the same as in the group with shockable rhythm. Survival outcomes in the group with non-shockable rhythm are lower than those with shockable rhythm in previous studies [34–36]. However, several studies support the observed trend that OHCA patients with a first recorded rhythm of PEA have significantly higher survival rates than those presenting with asystole [37–40]. “Pseudo-PEA”, or “pulseless with a rhythm with echocardiographic motion

Table 2. Multivariable logistic regression of survival to hospital discharge and neurological outcome with predictor of each minute of ALS response time.

|                          | Any ALS | Only ALS | ALS+BLS |
|--------------------------|---------|----------|---------|
| **Survival to hospital discharge (N = 287)** | (STHD/total) | Adjusted OR | (STHD/total) | Adjusted OR | (STHD/total) | Adjusted OR (95% CI) | Adjusted OR (95% CI) |
| All OHCA patients        | 287/4,278 | 0.93 (0.89–0.97) | 69/661 | 0.94 (0.82–1.07) | 218/3,617 | 0.94 (0.90–0.99) |
| Shockable rhythm (pVT/Vf) | 122/436 | 0.91 (0.89–0.97) | 31/88 | 0.79 (0.61–1.04) | 91/348 | 0.91 (0.85–0.99) |
| Non-shockable rhythm     | 165/3,842 | 0.94 (0.89–0.99) | 38/573 | 0.97 (0.83–1.13) | 127/3,269 | 0.96 (0.91–1.01) |
| PEA                      | 87/800 | 0.91 (0.85–0.98) | 20/154 | 0.87 (0.66–1.14) | 67/646 | 0.91 (0.83–0.99) |
| Asystole                 | 78/3,018 | 0.98 (0.91–1.05) | 18/415 | 1.05 (0.86–1.27) | 60/2,603 | 1.01 (0.94–1.08) |
| **CPC1–CPC2 (N = 126)** | (CPC1-2/total) | (CPC1-2/total) | (CPC1-2/total) | (CPC1-2/total) | 
| All OHCA patients        | 126/4,278 | 0.91 (0.85–0.97) | 36/661 | 0.92 (0.76–1.12) | 90/3,617 | 0.93 (0.87–0.997) |
| Shockable rhythm (pVT/Vf) | 80/436 | 0.89 (0.81–0.96) | 28/88 | 0.86 (0.67–1.11) | 52/348 | 0.92 (0.83–1.01) |
| Non-shockable rhythm     | 46/3,842 | 0.94 (0.85–1.03) | 8/573 | 0.93 (0.66–1.30) | 38/3,269 | 0.95 (0.86–1.05) |
| PEA                      | 33/800 | 0.88 (0.78–0.996) | 7/154 | 0.92 (0.62–1.37) | 26/646 | 0.88 (0.77–1.01) |
| Asystole                 | 13/3,018 | 1.06 (0.96–1.17) | 1/415 | NA | 12/2,603 | 1.04 (0.93–1.17) |

*: Adjusted by EMS response time, total EMT, age, sex, witness, bystander CPR, shockable rhythm.

**: Adjusted by EMS response time, total EMT, age, sex, witness, bystander CPR, shockable rhythm.

**: Adjusted by total EMT, age, sex, witness, bystander CPR, shockable rhythm.

**: Adjusted by total EMT, age, sex, witness, bystander CPR.

**: All observations have the same response.

*: P-value <0.05

ALS: advanced life support. BLS: basic life support. CPC: cerebral performance category. OHCA: out-of-hospital cardiac arrest. pVT: pulseless ventricular tachycardia.

PEA: pulseless electrical activity. VF: ventricular fibrillation

https://doi.org/10.1371/journal.pone.0266969.t002
"PREM)”, which refers to patients with PEA but a beating heart under ultrasound, could be the cause. Studies reveal that patients with PREM had higher survival rates than those with PEA without echocardiographic motion; aggressive ALS treatment may increase their survival [41–43].

![Spline curves for the outcomes of survival to hospital discharge (with 95% confidence intervals), as a function of ALS response time. Abbreviations: ALS = advanced life support. STHD = survival to hospital discharge.](https://doi.org/10.1371/journal.pone.0266969.g002)
There are several reasonable explanations for early ALS team response time improving the rate of survival to hospital discharge and neurological outcome among OHCA patients. ALS treatment includes airway management and drug administration. Network meta-analysis of randomized control trials reveal that ET tube placement and supraglottic airway (SGA) do increase the rate of ROSC compared to BVM [44]; the success rate of intubation greatly influenced the results. In one randomized clinical trial from Taipei EMS, among patients with OHCA, the initial airway management with ETI by ALS was associated with a higher probability of prehospital ROSC compared with SGA, especially among the subgroups of non-shockable rhythm, nonpublic collapse, arrested witnessed, call to airway time less than 14 minutes, and age 77 years or older, indicating that the shorter ALS response time may be related to a better chance of prehospital ROSC [45]. Chiang et al. [23] also found that successful out-of-hospital intubation with OHCA patients increased the odds of sustained ROSC, survival to hospital discharge, and favorable neurological outcome compared to BVM. With regard to adrenaline administration, Perkin et al. [16] reported that a prehospital adrenaline injection increases survival in OHCA patients by 30 days and further analysis reveals that an early injection of adrenaline can increase the probability of ROSC and survival to 30 days [46, 47]. Several studies also demonstrate that a delayed adrenaline injection might decrease the rate of survival to hospital discharge in OHCA patients and favorable neurological outcomes in non-shockable OHCA patients [48–50]. Furthermore, previous studies in the Taipei area show that the ALS team can enhance outcomes in OHCA patients. Ma et al. [24] found that an ALS team can improve ROSC and survival to admission. Sun et al. [25] found that an on-scene EMT–paramedics ratio > 50% is associated with improved survival to hospital discharge for OHCA cases, especially for those with witnessed, non-shockable rhythm. In addition, the awareness of OHCA management among the EMT is increasing and the ALS crews are more experienced,
good at teamwork, and enthusiastic [24]. Paramedics with a 5-year OHCA case volume of \( \geq 15 \) are significantly associated with ROSC [51], and in Taipei, one paramedic treated almost all of the 10 OHCA patients in 1 year [24]. Several studies have demonstrated that more experienced paramedics can improve the outcomes of OHCA patients [52, 53].

Some studies have opposed ALS treatment. The OPALS study compared the before and after of implementation of ALS paramedics into EMS in Canada. The results revealed no improvement in the rate of survival to hospital discharge and functional outcome in OHCA patients after ALS intervention [54]. Although by far the best evidence, the before and after study design and the lack of familiarity and clinical experience of newly-trained ALS crews could partially explain the results. The change in ALS treatment over the years may also improve patient outcomes. Sanghavi et al. [55] compared the BLS and ALS treatment in non-traumatic OHCA patients using a nationally representative sample of traditional Medicare beneficiaries from nonrural counties in the United States, and found that the ALS group was associated with poor neurological and survival outcomes. Using Medicare beneficiaries’ data could result in reporting bias and an overestimation of mortality [56]. A lack of at-scene data and ALS arrival time may also influence the results, as our study demonstrated that the time of ALS intervention was an important factor affecting outcomes. The use of national data could increase external validity while decreasing internal validity because the EMS systems, dispatchers, and paramedics are distinct from others in different states or areas. Michelland et al. [22] compared the early and late ALS arrivals in non-traumatic OHCA patients using propensity score matches in France, and found that early ALS intervention was associated with a lower rate of ROSC and neurological outcome at discharge after matching. The average arrival time of the ALS team in the early ALS group was 15 minutes in Michelland’s study, while our study revealed that the effect of ALS intervention diminished if the ALS response time was longer than 11 minutes. Grunau et al. [20] also demonstrated that the optimal cut-off time for ALS intervention was 10 minutes. In addition, the BLS team arrival time was shorter in the delayed ALS group than in the early ALS group (10 minutes vs. 13 minutes), which could have also affected the results.

Limitations

Our study had several limitations. First, this was a retrospective observational study. While selection bias inherent to our study design cannot be eliminated, we believe it was mitigated by our population-based approach. While we adjusted for common OHCA confounders, additional unmeasured or unmeasurable confounders may have been present, such as in-hospital care, which may have influenced OHCA survival [31, 57]. Second, we did not compare the difference between the ALS and only-BLS groups as the response time gap was close, and the BLS-only group may have included a higher proportion of patients who achieved rapid ROSC with defibrillation. Third, our study subjects were identified from the metropolitan regions of one Taiwanese city; causality, logistical, political, and ethical complexities in different settings may have limited the external validity. Furthermore, we examined the effect of ALS care on OHCA; other disease states were not discussed.

Conclusion

In non-traumatic, adult, OHCA patients in Taipei, a longer ALS response time was associated with worse odds of survival to hospital discharge and favorable neurological outcomes, especially in patients presenting with shockable rhythm and PEA.

Our study further suggests the optimal ALS response time for the EMS system.
Supporting information

S1 Table. Univariate logistic regression of survival to hospital discharge in each group. ALS: advanced life support. BLS: basic life support. CPR: cardiopulmonary resuscitation. EMS: emergency medical service. EMT: emergency medical technician. OHCA: out-of-hospital cardiac arrest. OR: odds ratio. pVT: pulseless ventricular tachycardia. PEA: pulseless electrical activity. STHD: survival to hospital discharge. VF: ventricular fibrillation.

S2 Table. Univariate logistic regression of CPC1–CPC2 in each group. ALS: advanced life support. BLS: basic life support. CPC: cerebral performance category. CPR: cardiopulmonary resuscitation. EMS: emergency medical service. EMT: emergency medical technician. OHCA: out-of-hospital cardiac arrest. OR: odds ratio. pVT: pulseless ventricular tachycardia. PEA: pulseless electrical activity. VF: ventricular fibrillation. a: cannot performed due to N = 1 in group CPC1-2.

Acknowledgments

The authors acknowledge the excellent performance of the EMT-Ps and the quality assurance of the Emergency Medical Service Division in Taipei City Fire Department, and their commitment and accomplishments, which significantly improve out-of-hospital care. The authors also like to thank the staff, Ms. Su-Mei Wang and Dr. Chin-Hao Chang, of the National Taiwan University Hospital Statistical Consulting Unit for help in statistical consultation.

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References

1. Wang CY, Wang JY, Teng NC, Chao TT, Tsai SL, Chen CL, et al. The secular trends in the incidence rate and outcomes of out-of-hospital cardiac arrest in Taiwan—a nationwide population-based study. PLoS One. 2015; 10(4):e0122675. https://doi.org/10.1371/journal.pone.0122675 PMID: 25875921

2. Ono Y, Hayakawa M, Iijima H, Maekawa K, Kodate A, Sadamoto Y, et al. The response time threshold for predicting favourable neurological outcomes in patients with bystander-witnessed out-of-hospital cardiac arrest. Resuscitation. 2016; 107:55–70. https://doi.org/10.1016/j.resuscitation.2016.08.005 PMID: 27531022

3. De Maio VJ, Stiell IG, Wells GA, Spaite DW, Ontario Prehospital Advanced Life Support Study G. Optimal defibrillation response intervals for maximum out-of-hospital cardiac arrest survival rates. Ann Emerg Med. 2003; 42(2):242–50. https://doi.org/10.1067/mem.2003.266 PMID: 12883512

4. Earnest A, Hock Ong ME, Shahidah N, Min Ng W, Foo C, Nott DJ. Spatial analysis of ambulance response times related to prehospital cardiac arrests in the city-state of Singapore. Prehosp Emerg Care. 2012; 16(2):256–65. https://doi.org/10.3109/10903127.2011.615974 PMID: 21999815

5. Gold LS, Fahrenbruch CE, Rea TD, Eisenberg MS. The relationship between time to arrival of emergency medical services (EMS) and survival from out-of-hospital ventricular fibrillation cardiac arrest. Resuscitation. 2010; 81(5):622–5. https://doi.org/10.1016/j.resuscitation.2010.02.004 PMID: 20207470

6. Pell JP, Sirel JM, Marsden AK, Ford I, Cobb SM. Effect of reducing ambulance response times on deaths from out of hospital cardiac arrest: cohort study. BMJ. 2001; 322(7299):1385–8. https://doi.org/10.1136/bmj.322.7299.1385 PMID: 11977420

7. O’Keeffe C, Nicholl J, Turner J, Goodacre S. Role of ambulance response times in the survival of patients with out-of-hospital cardiac arrest. Emerg Med J. 2011; 28(8):703–6. https://doi.org/10.1136/ emj.2009.086363 PMID: 20798090

8. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. Circulation. 1997; 96(10):3308–13. https://doi.org/10.1161/01.cir.96.10.3308 PMID: 9396421

9. Goto Y, Funada A, Goto Y. Relationship Between Emergency Medical Services Response Time and Bystander Intervention in Patients With Out-of-Hospital Cardiac Arrest. J Am Heart Assoc. 2018; 7(9). https://doi.org/10.1161/JAHA.1016.00829.x PMID: 20836772

10. Pell JP, Sirel JM, Marsden AK, Ford I, Cobb SM. Effect of adrenaline on survival in out-of-hospital cardiac arrest. Acad Emerg Med. 2010; 17(9):926–31. https://doi.org/10.1111/j.1553-2712.2010.00829.x PMID: 20836772

11. Wang HE, Schmicker RH, Daya MR, Stephens SW, Idris AH, Carlson JN, et al. Effect of a Strategy of Initial Laryngeal Tube Insertion vs Endotracheal Intubation on 72-Hour Survival in Adults With Out-of-
Hospital Cardiac Arrest: A Randomized Clinical Trial. Jama. 2018; 320(8):769–78. https://doi.org/10.1001/jama.2018.7044 PMID: 30167699

20. Grunau B, Kawano T, Scheuemeyer F, Tallon J, Reynolds J, Besserer F, et al. Early advanced life support attendance is associated with improved survival and neurologic outcomes after non-traumatic out-of-hospital cardiac arrest in a tiered prehospital response system. Resuscitation. 2019; 135:137–44. https://doi.org/10.1016/j.resuscitation.2018.12.003 PMID: 30576783

21. Kurz MC, Schmicker RH, Leroux B, Nichol G, Aufderheide TP, Cheskes S, et al. Advanced vs. Basic Life Support in the Treatment of Out-of-Hospital Cardiopulmonary Arrest in the Resuscitation Outcomes Consortium. Resuscitation. 2018; 128:132–7. https://doi.org/10.1016/j.resuscitation.2018.04.031 PMID: 29723609

22. Michelland L, Adnet F, Escunetaine J, Baker C, Hubert H, Chevret S. Association between early advanced life support and good neurological outcome in out of hospital cardiac arrest: A propensity score analysis. J Eval Clin Pract. 2020; 26(3):1013–21. https://doi.org/10.1111/jep.13268 PMID: 31466139

23. Chiang WC, Hsieh MJ, Chu HL, Chen AY, Yang WS, et al. The Effect of Successful Intubation on Patient Outcomes After Out-of-Hospital Cardiac Arrest in Taipei. Amn Emerg Med. 2018; 71(3):387–96.e2. https://doi.org/10.1016/j.annemergmed.2017.08.008 PMID: 28967516

24. Ma MH, Chiang WC, Ko PC, Huang JC, Lin CH, Wang HC, et al. Outcomes from out-of-hospital cardiac arrest in Metropolitan Taipei: does an advanced life support service make a difference? Resuscitation. 2007; 74(3):461–9. https://doi.org/10.1016/j.resuscitation.2007.02.006 PMID: 17462809

25. Sun JT, Chiang WC, Hsieh MJ, Huang EP, Yang WS, Chien YC, et al. The effect of the number and level of emergency medical technicians on patient outcomes following out of hospital cardiac arrest in Taipei. Resuscitation. 2018; 122:48–53. https://doi.org/10.1016/j.resuscitation.2017.11.048 PMID: 29169910

26. Chiang WC, Chen SY, Ko PC, Hsieh MJ, Wang HC, Huang EP, et al. Prehospital intravenous epinephrine may boost survival of patients with traumatic cardiac arrest: a retrospective cohort study. Scand J Trauma Resusc Emerg Med. 2015; 23:102. https://doi.org/10.1186/s13049-015-0181-4 PMID: 26585517

27. Tsai BM, Sun J-T, Hsieh M-J, Lin Y-Y, Kao T-C, Chen L-W, et al. Optimal paramedic numbers in resuscitation of patients with out-of-hospital cardiac arrest: A randomized controlled study in a simulation setting. PLOS ONE. 2020; 15(7):e0235315. https://doi.org/10.1371/journal.pone.0235315 PMID: 32634172

28. Chiang WC, Ko PC, Wang HC, Yang CW, Shih FY, Hsiung KH, et al. EMS in Taiwan: past, present, and future. Resuscitation. 2009; 80(1):9–13.

29. Brain Resuscitation Clinical Trial IISG. A randomized clinical study of a calcium-entry blocker (lidoflazine) in the treatment of comatose survivors of cardiac arrest. N Engl J Med. 1991; 324(18):1225–31. https://doi.org/10.1056/NEJM199105023241801 PMID: 15557386

30. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med. 2002; 346(8):549–56. https://doi.org/10.1056/NEJMoa012689 PMID: 11856793

31. Nielsen N, Wettterslev J, Cronberg T, Erlinge D, Gasche Y, Hassager C, et al. Targeted temperature management at 33˚C versus 36˚C after cardiac arrest. N Engl J Med. 2013; 369(23):2197–206. https://doi.org/10.1056/NEJMoa1305159 PMID: 24237006

32. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, 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 Councils of Southern Africa). Circulation. 2004; 110(21):3385–97. https://doi.org/10.1161/01.CIR.0000147236.85306.15 PMID: 15557386

33. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: A Statement for Healthcare Professionals From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Resuscitation. 2015; 96:328–40. https://doi.org/10.1016/j.resuscitation.2014.11.002 PMID: 25438254

34. Hawkes C, Booth S, Ji C, Brace-McDonnell SJ, Whittington A, Mapstone J, et al. Epidemiology and outcomes from out-of-hospital cardiac arrests in England. Resuscitation. 2017; 110:133–40. https://doi.org/10.1016/j.resuscitation.2016.10.030 PMID: 27865775
35. Herlitz J, Svensson L, Engdahl J, Sillverstolpe J. Characteristics and outcome in out-of-hospital cardiac arrest when patients are found in a non-shockable rhythm. Resuscitation. 2008; 76(1):31–6. https://doi.org/10.1016/j.resuscitation.2007.06.027 PMID: 17709164

36. McNally B, Robb R, Mehta M, Veliano K, Valderrama AL, Yoon PW, 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(8):1–19. PMID: 21796098

37. Andrew E, Nehme Z, Lijovic M, Bernard S, Smith K. Outcomes following out-of-hospital cardiac arrest with an initial cardiac rhythm of asystole or pulseless electrical activity in Victoria, Australia. Resuscitation. 2014; 85(11):1633–9. https://doi.org/10.1016/j.resuscitation.2014.07.015 PMID: 25110246

38. Fukuda T, Matsubara T, Doi K, Fukuda-Ohashi N, Yahagi N. Predictors of favorable and poor prognosis in witnessed out-of-hospital cardiac arrest with a non-shockable initial rhythm. Int J Cardiol. 2014; 176(3):910–5. https://doi.org/10.1016/j.ijcard.2014.08.057 PMID: 25168100

39. Ko DT, Qiu F, Koh M, Dorian P, Cheskes S, Austin PC, et al. Factors associated with out-of-hospital cardiac arrest with pulseless electrical activity: A population-based study. Am Heart J. 2016; 177:129–37. https://doi.org/10.1016/j.ahj.2016.04.018 PMID: 27297858

40. Bergstrom M, Schmidbauer S, Herlitz J, Rawshani A, Friberg H. Pulseless electrical activity is associated with improved survival in out-of-hospital cardiac arrest with initial non-shockable rhythm. Resuscitation. 2018; 133:147–52. https://doi.org/10.1016/j.resuscitation.2018.10.018 PMID: 30352246

41. Flato UA, Paiva EF, Carballo MT, Buehler AM, Marco R, Timerman A. Echocardiography for prognostication during the resuscitation of intensive care unit patients with non-shockable rhythm cardiac arrest. Resuscitation. 2015; 92:1–6. https://doi.org/10.1016/j.resuscitation.2015.03.024 PMID: 25891961

42. Wu C, Zheng Z, Jiang L, Gao Y, Xu J, Jin X, et al. The predictive value of bedside ultrasound to restore spontaneous circulation in patients with pulseless electrical activity: A systematic review and meta-analysis. PLoS One. 2018; 13(1):e0191636. https://doi.org/10.1371/journal.pone.0191636 PMID: 29364925

43. Gaspari R, Weekes A, Adhikari S, Noble VE, Nomura JT, Theodoro D, et al. Emergency department point-of-care ultrasound in out-of-hospital and in-ED cardiac arrest. Resuscitation. 2016; 109:33–9. https://doi.org/10.1016/j.resuscitation.2016.09.016 PMID: 27693280

44. Wang CH, Lee AF, Chang WT, Huang CH, Tsai MS, Chou E, et al. Comparing Effectiveness of Initial Airway Interventions for Out-of-Hospital Cardiac Arrest: A Systematic Review and Network Meta-analysis of Clinical Controlled Trials. Ann Emerg Med. 2020; 75(5):627–36. https://doi.org/10.1016/j.annemergmed.2019.12.003 PMID: 31983493

45. Lee A-F, Chien Y-C, Lee B-C, Yang W-S, Wang Y-C, Lin H-Y, et al. Effect of Placement of a Supraglottic Airway Device vs Endotracheal Intubation on Return of Spontaneous Circulation in Adults With Out-of-Hospital Cardiac Arrest in Taipei, Taiwan. JAMA Network Open. 2022; 5(2):e2148871. https://doi.org/10.1001/jamanetworkopen.2021.48871 PMID: 35178588

46. Perkins GD, Kenna C, Ji C, Deakin CD, Nolan JP, Quinn T, et al. The influence of time to adrenaline administration in the Paramedic 2 randomised controlled trial. Intensive Care Med. 2020; 46(3):426–36. https://doi.org/10.1007/s00134-019-05836-2 PMID: 31912202

47. Ran L, Liu J, Tanaka H, Hubble MW, Hiroshi T, Huang W. Early Administration of Adrenaline for Out-of-Hospital Cardiac Arrest: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2020; 9(11):e014330. https://doi.org/10.1161/JAHA.119.014330 PMID: 32441184

48. Hansen M, Schmicker RH, Newsgrad GD, Grunau B, Scheuemeyer F, Cheskes S, et al. Time to Epinephrine Administration and Survival From Nonshockable Out-of-Hospital Cardiac Arrest Among Children and Adults. Circulation. 2018; 137(19):2032–40. https://doi.org/10.1161/CIRCULATIONAHA.117.033067 PMID: 29511001

49. Homma Y, Shiga T, Funakoshi H, Miyazaki D, Sakurai A, Tahara Y, et al. Association of the time to first epinephrine administration and outcomes in out-of-hospital cardiac arrest: SOS-KANTO 2012 study. Am J Emerg Med. 2019; 37(2):241–8. https://doi.org/10.1016/j.ajem.2018.05.037 PMID: 29804789

50. Sigal AP, Sandel KM, Buckler DG, Wasser T, Abella BS. Impact of adrenaline dose and timing on out-of-hospital cardiac arrest survival and neurological outcomes. Resuscitation. 2019; 139:182–8. https://doi.org/10.1016/j.resuscitation.2019.04.018 PMID: 30991079

51. Tuttle JE, Hubble MW. Paramedic Out-of-hospital Cardiac Arrest Case Volume Is a Predictor of Return of Spontaneous Circulation. West J Emerg Med. 2018; 19(4):654–9. https://doi.org/10.5811/westjem.2018.3.37051 PMID: 30013700

52. Gold LS, Eisenberg MS. The effect of paramedic experience on survival from cardiac arrest. Prehosp Emerg Care. 2009; 13(3):341–4. https://doi.org/10.1080/10903120902935389 PMID: 19499471

53. Wang HE, Balasubramani GK, Cook LJ, Lave JR, Yealy DM. Out-of-hospital endotracheal intubation experience and patient outcomes. Ann Emerg Med. 2010; 55(6):527–37 e6. https://doi.org/10.1016/j.annemergmed.2009.12.020 PMID: 2138400
54. Stiell IG, Wells GA, Field B, Spaite DW, Nesbitt LP, De Maio VJ, et al. Advanced Cardiac Life Support in Out-of-Hospital Cardiac Arrest. New England Journal of Medicine. 2004; 351(7):647–56.

55. Sanghavi P, Jena AB, Newhouse JP, Zaslavsky AM. Outcomes after out-of-hospital cardiac arrest treated by basic vs advanced life support. JAMA Intern Med. 2015; 175(2):196–204. https://doi.org/10.1001/jamainternmed.2014.5420 PMID: 25419698

56. Coppler PJ, Rittenberger JC, Callaway CW, Elmer J. Billing diagnoses do not accurately identify out-of-hospital cardiac arrest patients: An analysis of a regional healthcare system. Resuscitation. 2016; 98:9–14. https://doi.org/10.1016/j.resuscitation.2015.09.399 PMID: 26476197

57. Larsen JM, Ravkilde J. Acute coronary angiography in patients resuscitated from out-of-hospital cardiac arrest—a systematic review and meta-analysis. Resuscitation. 2012; 83(12):1427–33. https://doi.org/10.1016/j.resuscitation.2012.08.337 PMID: 22960567