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The influences of adrenaline dosing frequency and dosage on outcomes of adult in-hospital cardiac arrest: A retrospective cohort study☆

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ABSTRACT

Aim: To investigate the influence of dosing frequency and dosage of adrenaline on outcomes of cardiopulmonary resuscitation (CPR).
Methods: We conducted a retrospective observational study in a single medical centre and included adult patients who had suffered an in-hospital cardiac arrest between 2006 and 2012. We used multivariable logistic regression analysis to evaluate the associations between independent variables and outcomes. Adrenaline average dosing frequency was calculated as the total dosage of adrenaline administered during CPR divided by the duration of CPR. Body weight (BW) was analysed as an interaction term to investigate the effect of adrenaline dosage on outcomes. Favourable neurological outcome was defined as a score of 1 or 2 on the Cerebral Performance Category scale at hospital discharge.
Results: We included 896 patients in the analysis. After adjusting for multiple confounding factors, including CPR duration, the results indicated that higher adrenaline dosing frequency was associated with lower rates of survival (odds ratio (OR): 0.05, 95% confidence interval (CI): 0.01–0.23) and favourable neurological outcome at hospital discharge (OR: 0.02, 95% CI: 0.002–0.16). A significant interaction was noted between total adrenaline dosage and BW, which indicated that, with the same adrenaline dosage, the outcomes for patients with BW $\geq$ 82.5 kg would be worse than those for patients with lower BW.
Conclusion: Higher adrenaline average dosing frequency may be associated with worse outcomes after CPR. Besides, according to current recommendations, patients with BW above 82.5 kg may not receive adequate dose of adrenaline.

Introduction

Advanced life support during cardiac arrest management comprises cardiopulmonary resuscitation (CPR), defibrillation, airway management, and administration of vasoactive drugs.[1–3] As a potent vasopressor, adrenaline (epinephrine) has been an integral component of advanced life support since the inception of modern CPR in the early 1960s.[4]

The alpha-adrenergic effects of adrenaline produce systemic vasoconstriction, increasing coronary and cerebral perfusion pressures, which are believed to be beneficial in achieving return of spontaneous circulation (ROSC). However, some adverse effects of adrenaline administration have also been observed in animal studies, including increased myocardial oxygen consumption[5] and reduced cerebral microcirculatory blood flow,[6]

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which might lead to long-term mortality associated with cardiac arrest.[7,8]

For out-of-hospital cardiac arrest (OHCA), several studies have reported that the results associated with adrenaline administered by emergency medical staff in the prehospital setting were either worse or, at best, equivalent to CPR without the administration of adrenaline.[9–12] No similar studies have been conducted for patients who suffer in-hospital cardiac arrest (IHCA).

Current guidelines recommend 1 mg of adrenaline administered every 3 to 5 min during CPR. While the effects of adrenaline dosing frequency could be directly analysed, it might be difficult to investigate the effect of adrenaline dosage directly since during CPR, most physicians would administer a fixed dose of adrenaline for each injection.[1–3] In most animal studies,[13–17] weight-based doses, rather than a fixed dose, of adrenaline were used for CPR. Therefore, we included body weight (BW) in the analysis to observe the effect of adrenaline dosage on CPR outcome in an indirect manner.

Materials and methods

Setting

We conducted a retrospective cohort study at the National Taiwan University Hospital (NTUH), which is a tertiary care centre. The study was performed in accordance with the amended Declaration of Helsinki. Prior to data collection, the Institutional Review Board of the NTUH approved this study (reference number: 201508038RIN) and for this type of study, formal consent is not required. The NTUH has 2600 beds, including 220 beds in intensive care units (ICUs). According to hospital policy, a code team is activated when a cardiac arrest event occurs in the general wards. A code team consists of a senior resident, several junior residents, a respiratory therapist, a head nurse, and several registered nurses from the ICUs. Each code team member has been certified to provide advanced life support according to AHA/ILCOR resuscitation guidelines. When a cardiac arrest event occurs in the ICUs, resuscitation is performed by the staff of the ICU where the cardiac arrest event occurred and by staff from neighbouring ICUs.

Participants

We included patients who had suffered an IHCA at the NTUH between 2006 and 2012. We included patients who met the following criteria: (1) age $\geq$18 years; (2) documented absence of pulse with performance of chest compression for $\geq$2 min; and (3) no documentation of a do-not-resuscitate order. If multiple cardiac arrest events occurred in a single patient, we only recorded the first event of the same hospitalization. We excluded patients who had suffered a cardiac arrest related to major trauma. We also excluded patients without measurements of BW.

Data collection and outcome measures

We abstracted the following information for each patient from the routine medical records: demographics, actual BW measured on admission, comorbidities (see definitions in Supplemental Table 1), variables derived from the Utstein template,[18] and any critical intervention that was implemented at the time of cardiac arrest or after ROSC. The timing of the CPR process was recorded by the nursing member of the code team according to hospital-regulated protocols. The times were recorded according to hospital-wide clocks which were checked every day to ensure the times were unified across the hospital. CPR duration was defined as the time from the first chest compression provided by the code team or ICU members to the termination of resuscitation efforts, either due to sustained ROSC or declaration of death. Adrenaline average dosing frequency was calculated as total adrenaline dosage administered during CPR divided by CPR duration.[19]

The primary outcome was survival to hospital discharge. Secondary outcomes included sustained ROSC, survival for 24 h, and favourable neurological status at hospital discharge, which was defined as a score of 1 or 2 on the Cerebral Performance Category (CPC) scale.[20] We retrospectively determined the CPC score by reviewing medical records for each patient.

Statistical analysis

We used R 2.15.3 software (R Foundation for Statistical Computing, Vienna, Austria) for data analysis. Categorical data were expressed as counts and proportions; continuous data were expressed as means and standard deviations. Categorical variables were compared by the Fisher's exact test, and continuous variables were examined by the Wilcoxon rank-sum test. A two-tailed p-value of $\leq$0.05 was considered statistically significant.

We selected the odds ratio (OR) as the outcome measure. We conducted a multivariable logistic regression analysis to examine the association between variables and outcomes. CPR duration was analysed as an independent variable to decrease the possibility of confounding by indication. BW was analysed as an interaction term with adrenaline average dosing frequency to observe the effect of adrenaline dosage on outcomes.

All available independent variables, including interaction terms, were considered in the regression model, regardless of whether they were significant by univariate analysis. The stepwise variable selection procedure (with iterations between the forward and backward steps) was applied to obtain the final regression model. Significance levels for entry and to stay were set at 0.15 to avoid exclusion of potential candidate variables. The final regression model was identified by excluding individual variables with a p-value >0.05, until all regression coefficients were statistically significant.

We used generalized additive models (GAMs)[21] to examine the nonlinear effects of continuous variables on outcomes and, if necessary, to identify the appropriate cut-off point(s) for dichotomizing a continuous variable during the variable selection procedure. We also used conditional effect plots[22] to visualize the predicted probability of outcomes against variables of interest while the other independent variables in the final model remained constant. We assessed the goodness-of-fit of the fitted regression model using c statistics, adjusted generalized R^2, and the Hosmer–Lemeshow goodness-of-fit test.

Results

We identified a total of 1114 patients met the inclusion criteria for our study. Of these, 9 patients were excluded because of trauma-related cardiac arrest, and 209 patients were excluded because of lack of measurement of BW. The remaining 896 patients were included for further analysis.

The characteristics of the included patients, stratified by primary outcome, are presented in Tables 1 and 2. The mean BW was 60.1 kg. Shockable rhythms represented 14.5% of initial arrest rhythms. The mean total dosage of adrenaline administered during CPR was 8.1 mg and the mean duration of CPR was 33.3 min. The mean adrenaline average dosing frequency was 0.28 mg/min. Only 140 patients (15.6%) survived to hospital discharge and 74 of these patients (8.3%) displayed a favourable neurological status.

All independent variables listed in Tables 1 and 2 were included in the variable selection procedure for the primary outcome. The GAM plot that is shown in Supplemental Fig. 1 revealed that logit (p), where p represented the probability for survival to hospital

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Table 1
Baseline characteristics of study patients stratified by primary outcome.

Variables	All patients (n = 896)	Survival to hospital discharge (n = 140)	Death at hospital discharge (n = 756)	p-Value
Age, y (SD[a])	64.3 (17.2)	64.7 (16.2)	64.3 (17.4)	0.81
Male, n (%)	567 (63.3)	95 (67.9)	472 (62.4)	0.25
Body weight, kg (SD)	60.1 (14.2)	59.7 (12.6)	60.2 (14.5)	0.86
Comorbidities, n (%)				
Heart failure	235 (26.2)	38 (27.1)	197 (26.1)	0.83
Myocardial infarction	114 (12.7)	30 (21.4)	84 (11.1)	0.001
Arrhythmia	141 (15.7)	28 (20.0)	113 (14.9)	0.13
Hypotension	172 (19.2)	17 (12.1)	155 (20.5)	0.02
Respiratory insufficiency	643 (71.8)	88 (62.9)	555 (73.4)	0.01
Pneumonia	303 (33.8)	54 (38.6)	249 (32.9)	0.21
Renal insufficiency	363 (40.5)	49 (35.0)	314 (41.5)	0.16
Chronic dialysis	153 (17.1)	29 (20.7)	124 (16.4)	0.22
Hepatic insufficiency	158 (17.6)	9 (6.4)	149 (19.7)	<0.001
Metabolic or electrolyte abnormality	141 (15.7)	16 (11.4)	125 (16.5)	0.16
Diabetes mellitus	273 (30.5)	53 (37.9)	220 (29.1)	0.05
Baseline evidence of motor, cognitive, or functional deficits	181 (20.2)	30 (21.4)	151 (20.0)	0.73
Acute stroke	30 (3.3)	7 (5.0)	23 (3.0)	0.30
Favourable neurological status at admission	526 (58.7)	86 (61.4)	440 (58.2)	0.51
Favourable neurological status 24 h before cardiac arrest	373 (41.6)	75 (53.6)	298 (39.4)	0.002
Bacteraemia	91 (10.2)	15 (10.7)	76 (10.1)	0.76
Metastatic cancer or any blood borne malignancy	229 (25.6)	13 (9.3)	216 (28.6)	<0.001

[a] SD, standard deviation.

discharge, decreased gradually when BW was greater than 82.5 kg; the GAM plot that is shown in Supplemental Fig. 2 demonstrated the near-linear association between logit (p) and adrenaline average dosing frequency. If logit (p) was ≥0, the odds for survival were ≥1. Therefore, we selected a BW of 82.5 kg as the cut-off point to transform BW into a binary variable. The characteristics and outcomes of included patients, stratified by BW, are presented in Supplemental Tables 2 and 3.

The final regression model is shown in Table 3. Model A demonstrated that adrenaline average dosing frequency was inversely associated with survival to hospital discharge (OR: 0.05, 95% confidence interval: 0.01–0.23); model B indicated that there was a significant interaction between adrenaline average dosing frequency and BW. The conditional effect plot constructed according to model B (Fig. 1) demonstrated that when the total dosage of adrenaline administered during CPR (the product of CPR duration

Table 2
Features, interventions, and outcomes of cardiac arrest events stratified by primary outcome.

Variables	All patients (n = 896)	Survival to hospital discharge (n = 140)	Death at hospital discharge (n = 756)	p-Value
Arrest at night, n (%)	581 (64.8)	82 (58.6)	499 (66.0)	0.10
Arrest on weekend, n (%)	261 (29.1)	37 (26.4)	224 (29.6)	0.48
Arrest location, n (%)				0.62
Intensive care unit	417 (46.5)	65 (46.4)	352 (46.6)	
General ward	435 (48.5)	66 (47.1)	369 (48.8)	
Other	44 (4.9)	9 (6.4)	35 (4.6)	
Witnessed arrest, n (%)	627 (70.0)	94 (67.1)	533 (70.5)	0.42
Monitored status, n (%)	555 (61.9)	87 (62.1)	468 (61.9)	1
Shockable rhythm, n (%)	130 (14.5)	49 (35.0)	81 (10.7)	<0.001
Critical care interventions in place at time of arrest, n (%)				
Mechanical ventilation	166 (18.5)	22 (15.7)	144 (19.0)	0.41
Antiarrhythmics	92 (10.3)	17 (12.1)	75 (9.9)	0.45
Vasopressors	423 (47.2)	51 (36.4)	372 (49.2)	0.006
Dialysis	69 (7.7)	7 (5.0)	62 (8.2)	0.23
Pulmonary artery catheter	5 (0.6)	3 (2.1)	2 (0.3)	0.03
Intra-aortic balloon pumping	4 (0.4)	2 (1.4)	2 (0.3)	0.12
Total dosage of adrenaline, mg (SD[a])	8.1 (7.6)	3.2 (3.4)	9.1 (7.8)	<0.001
CPR[b] duration, min (SD)	33.3 (29.5)	13.6 (13.8)	36.9 (30.1)	<0.001
Adrenaline average dosing frequency, mg/min (SD)	0.28 (0.15)	0.26 (0.16)	0.28 (0.15)	0.02
Post-ROSC[c] interventions, n (%)				
Extracorporeal membrane oxygenation	54 (6.0)	13 (9.3)	41 (5.4)	0.08
Therapeutic hypothermia	2 (0.2)	0 (0)	2 (0.3)	1
Percutaneous coronary intervention	35 (3.9)	24 (17.1)	11 (1.5)	<0.001
Sustained ROSC, n (%)	510 (56.9)	140 (100)	370 (48.9)	<0.001
Survival for 24 h, n (%)	325 (36.3)	140 (100)	185 (24.5)	<0.001
Favourable neurological outcome at hospital discharge	74 (8.3)	74 (52.9)	0 (0)	<0.001

[a] SD, standard deviation.
[b] CPR, cardiopulmonary resuscitation.
[c] ROSC, return of spontaneous circulation.

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Table 3
Multiple logistic regression models with survival to hospital discharge as the dependent variable.

Independent variable[a]	Model A[d] without interaction terms			Model B[f] with interaction terms		
	Odds ratio	95% confidence interval	*p*-Value	Odds ratio	95% Confidence interval	*p*-Value
Male	1.62	1.02–2.62	0.04	1.73	1.09–2.80	0.02
Hepatic insufficiency	0.21	0.09–0.42	<0.001	0.20	0.09–0.40	<0.001
Favourable neurological status 24 h before cardiac arrest	1.97	1.25–3.13	0.004	2.25	1.44–3.52	<0.001
Metastatic cancer or any blood borne malignancy	0.31	0.16–0.58	<0.001	0.30	0.15–0.56	<0.001
Shockable rhythm	2.33	1.35–4.02	0.002	2.22	1.29–3.80	0.004
Vasopressors use at time of arrest	0.63	0.39–1.00	0.05	NA	NA	NA
CPR[b] duration	0.93	0.91–0.94	<0.001	0.93	0.91–0.94	<0.001
Adrenaline average dosing frequency	0.05	0.01–0.23	<0.001	NA	NA	NA
Adrenaline average dosing frequency × Body weight ≥ 82.5 kg	NA[e]	NA	NA	3.53×10^{-3}	3.00×10^{-5}–0.15	0.008
Adrenaline average dosing frequency × Body weight < 82.5 kg	NA	NA	NA	0.05	0.01–0.21	<0.001
Post-ROSC[c] percutaneous coronary intervention	6.75	2.59–19.27	<0.001	6.41	2.48–19.08	<0.001

[a] The display of independent variables is arranged by the order of these variables in Tables 1 and 2.
[b] CPR, cardiopulmonary resuscitation.
[c] ROSC, return of spontaneous circulation.
[d] Model A: Goodness-of-fit assessment: $n = 896$, adjusted generalized $R^2 = 0.43$, the estimated area under the receiver operating characteristic (ROC) curve = 0.87, and the Hosmer–Lemeshow chi-squared test p-value = 0.008.
[e] NA, not available.
[f] Model B: Goodness-of-fit assessment: $n = 896$, adjusted generalized $R^2 = 0.42$, the estimated area under the ROC curve = 0.87, and the Hosmer–Lemeshow chi-squared test p-value = 0.15.

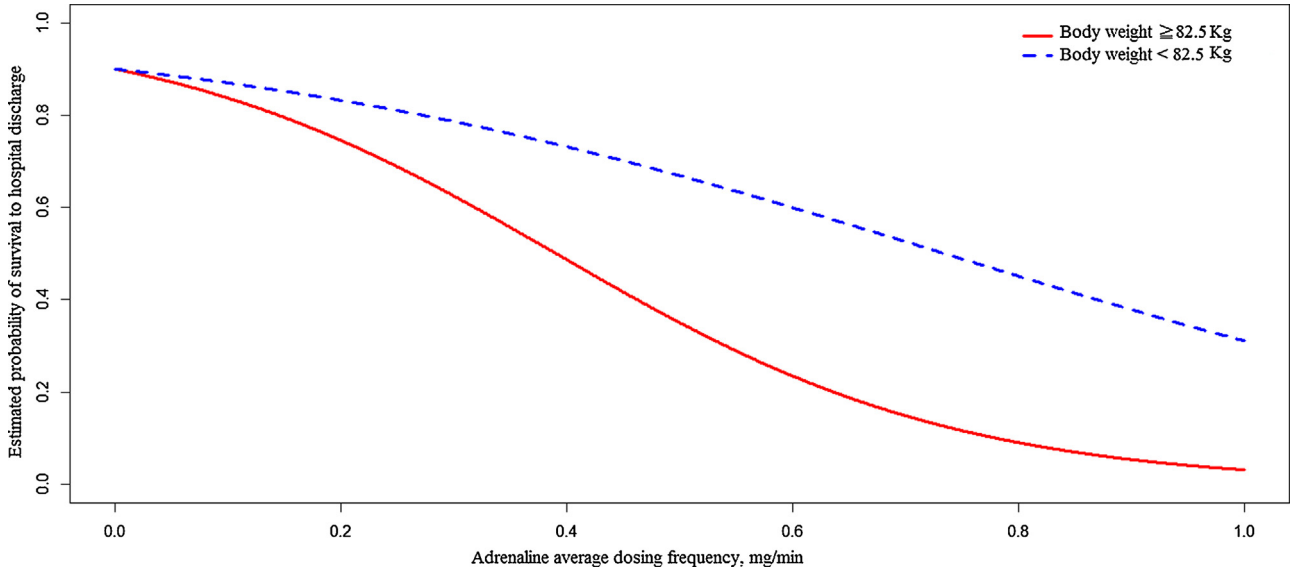

Fig. 1. Conditional effect plot of adrenaline average dosing frequency on the estimated probability of survival to hospital discharge. The plot was based on multiple logistic regression model B with the following settings: male (+), hepatic insufficiency (−), favourable neurological status 24 h before cardiac arrest (+), metastatic cancer or any blood borne malignancy (−), shockable rhythm (+), vasopressor use at time of arrest (−), CPR duration: 33.3 min, adrenaline average dosing frequency: 0.28 mg/min, Post-ROSC percutaneous coronary intervention (+).
CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation.

and adrenaline average dosing frequency) was the same, the survival probability for patients with BW ≥ 82.5 kg was lower than for patients with BW < 82.5 kg.

For secondary outcomes, except sustained ROSC, adrenaline dosing frequency was inversely associated with survival for 24 h and favourable neurological outcome at hospital discharge (Table 4, full models in Supplemental Tables 4–6).

Discussion

The results of this retrospective observational study indicate that higher adrenaline average dosing frequency might be associated with lower rates of survival and favourable neurological outcomes at hospital discharge after IHCA. Additionally, when the total dosage of adrenaline administered during CPR was the same, the outcomes for patients with BW ≥ 82.5 kg were worse than for patients with BW < 82.5 kg.

The current recommendations[1–3] for adrenaline dosing frequency (1 mg every 3 to 5 min) are based on expert opinion. In an animal study, Kosnik et al.[13] noted that a single high dose of adrenaline (0.15 mg/kg) could help dogs sustain diastolic blood pressure at 30 mmHg for approximately 10 min. Other animal studies[14,15] also indicated that a single high dose of adrenaline (0.2 mg/kg) maintained coronary perfusion pressure above baseline for longer than 5 min. These studies[13–15] suggest that a single administration of adrenaline might produce desired haemodynamic responses during CPR for longer than the recommended interval of repeated adrenaline administration (i.e. 3 to 5 min)[1–3] and that less frequent administration of adrenaline[1–3] may be acceptable.

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Table 4
Influence of adrenaline average dosing frequency on secondary outcomes after adjustment for multiple confounders.

Independent variable	Model[a] without interaction terms			Model[a] with interaction terms		
	Odds ratio	95% confidence interval	*p*-Value	Odds ratio	95% confidence interval	*p*-Value
Sustained ROSC[b]						
Adrenaline average dosing frequency	0.49	0.15–1.58	0.23	NA	NA	NA
Adrenaline average dosing frequency × Body weight ≥ 82.5 kg	NA[c]	NA	NA	1.00	0.10–11.08	1.00
Adrenaline average dosing frequency × Body weight < 82.5 kg	NA	NA	NA	0.47	0.15–1.52	0.20
Survival for 24 h						
Adrenaline average dosing frequency	0.04	0.01–0.14	<0.001	NA	NA	NA
Adrenaline average dosing frequency × Body weight ≥ 82.5 kg	NA	NA	NA	0.02	1.42×10^{-3}–0.28	0.004
Adrenaline average dosing frequency × Body weight < 82.5 kg	NA	NA	NA	0.04	0.01–0.14	<0.001
Favourable neurological outcome at hospital discharge						
Adrenaline average dosing frequency	0.02	2.00×10^{-3}–0.16	<0.001	NA	NA	NA
Adrenaline average dosing frequency × Body weight ≥ 82.5 kg	NA	NA	NA	7.16×10^{-7}	5.71×10^{-12}–2.03×10^{-3}	0.003
Adrenaline average dosing frequency × Body weight < 82.5 kg	NA	NA	NA	0.02	1.88×10^{-3}–0.16	<0.001

[a] The full models were available in Supplemental Tables 4–6.
[b] ROSC, return of spontaneous circulation
[c] NA, not available.

In an animal study that investigated repeated injections of adrenaline, Bar-Joseph et al.[16] reported a significant increase in systolic, diastolic, and coronary perfusion pressures after the first injection of high-dose adrenaline (0.1 mg/kg). No further significant increases in arterial pressures were observed in response to the next 3 doses of adrenaline, which were administered 5 min apart.[16] Cairns et al.[23] also demonstrated that multiple doses of adrenaline (1 mg/dose, approximately 0.04 mg/kg) had no statistically significant effects on coronary perfusion pressure. Possibly, multiple doses of adrenaline repeated at short intervals desensitized myocardial and peripheral adrenergic receptors[24] and led to diminished haemodynamic responses.

Only a few clinical studies have investigated the associations between adrenaline dosing frequency and outcomes. In a previous study of OHCA, Cantrell et al.[25] noted that there was no difference in the adrenaline average dosing frequency between patients who achieved ROSC and those who did not. Warren et al.[19] indicated that adrenaline average dosing that was less frequent than recommended by guidelines[1–3] was associated with improved survival to hospital discharge for IHCA patients. Our study not only corroborated the results of these studies[19,25] but also exposed the inverse association between adrenaline average dosing frequency and favourable neurological outcome. Further, Warren et al.[19] did not analyse the effects of adrenaline dosage in addition to dosing frequency. For our study, we considered total adrenaline dosage to be an important confounding factor in the analysis, and we revealed a significant interaction between BW and adrenaline dosage.

Few studies have investigated the influence of BW on CPR outcomes. For IHCA patients, Jain et al.[26] noted that the patterns of influence by body mass index (BMI) were different between patients with shockable and nonshockable rhythms: for shockable rhythms, overweight and obese patients had a higher rate of survival to discharge; in contrast, for nonshockable rhythms, survival to discharge was similar regardless of BMI, except for underweight patients with a lower survival rate. The GAM plot constructed during our analysis (Supplemental Fig. 1) demonstrated that the survival probability decreased proportionally with increasing BW when patients weighed more than 82.5 kg. Still, we detected no significant association between BW itself and outcomes, regardless of whether BW was transformed into a binary variable according to the cut-off point. One explanation for this finding might be that only 6.7% (60/896) of the total patient cohort had a BW ≥82.5 kg; this small proportion would have provided inadequate power to detect any differences between groups. Or, as suggested by Jain et al.,[26] this finding could have been due to the fact that associations between BW and CPR outcomes are confounded by the use and amount of adrenaline.

Adrenaline average dosing frequency was calculated by dividing the total dosage of adrenaline by CPR duration. Therefore, when we controlled the effects of average dosing frequency and CPR duration, we indirectly controlled the effects of adrenaline total dosage. The relationships among adrenaline average dosing frequency, dosage, CPR duration, and outcomes are better illustrated by the conditional effect plot, which was based on regression model B (Fig. 1). The CPR duration was specified as 33.3 min (i.e. the average CPR duration in our cohort) for Fig. 1. Fig. 1 indicates that when total adrenaline dosage is the same (i.e. when dosing frequency is the same), the survival probabilities would differ depending on the BWs of patients. This finding also suggests that the recommended total adrenaline dosage per kg might be insufficient for patients with BW ≥ 82.5 kg.

On the other hand, Fig. 1 also suggested that when adrenaline average dosing frequency increased (i.e. when total adrenaline dosage increased), the survival probabilities would decrease for both patient groups irrespective of their BW. Therefore, for patients with BW ≥ 82.5 kg, instead of increasing the adrenaline average dosing frequency to complement the inadequate adrenaline dosage, clinicians may consider increasing the adrenaline dosage of each single shot. This conclusion was also in line with the results of previous animal studies,[13–16,23] which suggested that a single weight-based dose of adrenaline may maintain the desired physiologic response longer than the recommended intervals[13–15] and repeated doses of adrenaline might be beneficial.[16,23]

In a series of studies, Friess et al.[27] and Sutton et al.[28,29] demonstrated that a CPR approach that is guided by haemodynamic responses improved short-term survival compared to current recommendations.[1–3] Specifically, in the haemodynamics-guided group, vasopressors, including adrenaline and vasopressin, were titrated to maintain a coronary perfusion pressure >20 mmHg.[27–29] These studies[27–29] indicate that administration of adrenaline according to coronary perfusion pressure during CPR would likely lead to improved outcomes compared to the fixed dosing frequency and amount of adrenaline recommended by the guidelines.[1–3]

In summary, we found that a higher adrenaline dosing frequency may be associated with worse outcomes after IHCA. Also, current recommendations for adrenaline dosages may be insufficient for patients with higher BW. Our results support the concept that CPR processes should be individualized according to each patient's needs and responses.[27–29] Especially for IHCA patients, who are often resuscitated in ICUs with the simultaneous monitoring of

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many physiologic parameters, CPR can possibly be performed and adrenaline can be administered in response to real-time feedback. A one-size-fits-all approach may not be appropriate for all CPR and cardiac arrest events.

Study limitations

First, this was an observational study, and, as such, we can only establish an association and not a causal relationship between independent and dependent variables. Second, the actual dosing frequency of adrenaline is erratic in clinical practice and is not as regular as the calculated average dosing frequency used in our analysis. The regularity of adrenaline dosing frequency might be in itself an important confounding factor, which we were not able to control in the analysis. Also, although the timing of the adrenaline was recorded by nursing staff according to hospital-regulated protocols, the data might still be incorrectly recorded because of the emergent situations. Third, intubation and use of antiarrhythmics during CPR might also influence the associations between BW and CPR outcomes. Because of the small number of patients included in current analysis, the effects of these two variables might be left for future studies to investigate. Fourth, like most retrospective studies involving cardiac arrest,[19] we were not able to control for the CPR quality, such as rate and depth of chest compressions, in the analysis. Finally, we used IHCA patients for our analysis. Further investigation is needed to confirm if our results can be applied to OHCA patients.

Conclusions

Higher adrenaline average dosing frequency may be associated with lower rates of survival and favourable neurological outcomes at hospital discharge after IHCA. Additionally, patients with BW above 82.5 kg may not receive adequate dose of adrenaline.

Conflict of interest statement

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2015.12.008.

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