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The impact of peri-shock pause on survival from out-of-hospital shockable cardiac arrest during the Resuscitation Outcomes Consortium PRIMED trial☆

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ABSTRACT

Background: Previous research has demonstrated significant relationships between peri-shock pause and survival to discharge from out-of-hospital shockable cardiac arrest (OHCA).
Objective: To determine the impact of peri-shock pause on survival from OHCA during the ROC PRIMED randomized controlled trial.
Methods: We included patients in the ROC PRIMED trial who suffered OHCA between June 2007 and November 2009, presented with a shockable rhythm and had CPR process data for at least one shock. We used multivariable logistic regression to determine the association between peri-shock pause duration and survival to hospital discharge.
Results: Among 2006 patients studied, the median (IQR) shock pause duration was: pre-shock pause 15 s (8, 22); post-shock pause 6 s (4, 9); and peri-shock pause 22.0 s (14, 31). After adjusting for Utstein predictors of survival as well as CPR quality measures, the odds of survival to hospital discharge were significantly higher for patients with pre-shock pause <10 s (OR: 1.52, 95% CI: 1.09, 2.11) and peri-shock pause <20 s (OR: 1.82, 95% CI: 1.17, 2.85) when compared to patients with pre-shock pause ≥20 s and peri-shock pause ≥40 s. Post-shock pause was not significantly associated with survival to hospital discharge. Results for neurologically intact survival (Modified Rankin Score ≤ 3) were similar to our primary outcome.
Conclusions: In patients with cardiac arrest presenting in a shockable rhythm during the ROC PRIMED trial, shorter pre- and peri-shock pauses were significantly associated with higher odds of survival. Future cardiopulmonary education and technology should focus on minimizing all peri-shock pauses.

1. Introduction

Survival from out-of-hospital cardiac arrest (OHCA) continues to challenge Emergency Medical Services (EMS) systems.[1–3] With an annual incidence of greater than 190,000 treated cardiac arrests per year in North America alone, the search continues for the components of resuscitation essential to improved

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survival. Historically, predictors of survival from OHCA such as the Utstein data elements, have focused on system (response time, time to first shock, bystander CPR, bystander witnessed state, public location) and patient (age, presence or absence of shockable rhythm) characteristics.[4] Previous research has demonstrated that Utstein variables alone are insufficient to accurately predict outcome from OHCA.[5] With the advent of the 2010 American Heart Association-International Liaison Committee on Resuscitation (AHA-ILCOR) guidelines for Cardiopulmonary Resuscitation (CPR), renewed interest has focused on improving survival through improvements in the characteristic components of cardiopulmonary resuscitation (CPR).[6,7]

CPR metrics such as peri-shock pause, chest compression fraction (CCF), chest compression depth, chest compression rate, and chest recoil may all impact cardiac arrest outcomes.[8–13] A previous study by the Resuscitation Outcomes Consortium (ROC) employing the Consortium's cardiac arrest registry database demonstrated a significant association between both pre- and peri-shock pause (PSP) duration and survival from shockable OHCA.[14] Limitations to this study include sample size, lack of participation by all ROC sites, lack of neurologically intact (Modified Rankin Score ≤3 or Cerebral Performance Category) outcome data, high rate of missing shock pause data as well as a regression model that did not control for other CPR metrics (CCF, compression depth and compression rate). In June 2007, ROC sites began enrolling patients in the Prehospital Resuscitation Impedance Valve and Early vs. Delayed Analysis Randomized Controlled trial known as ROC PRIMED.[15] Given the trial's size and its broad participation by all ROC sites, it provided a more robust data set to validate our previous findings. We therefore sought to estimate the strength of association between peri-shock pause duration and survival from shockable OHCA during the ROC PRIMED randomized controlled trial.

2. Methods

2.1. Setting and design

The ROC consists of 10 Regional Clinical Centers across North America, 7 in the United States (Pittsburgh, Pennsylvania; Dallas, Texas; Milwaukee, Wisconsin; Birmingham, Alabama; Seattle/King County, Washington; Portland, Oregon; and San Diego, California) and 3 in Canada (Toronto, Ontario; Vancouver, British Columbia and Ottawa, Ontario) as well as their respective EMS systems.[16,17] From June 2007 to November 2009, one hundred and fifty EMS agencies participated in the ROC PRIMED randomized controlled trial. A detailed description of the methods has been described previously.[18] The trial studied two different resuscitation strategies, a thirty second vs. a three minute CPR strategy prior to initial rhythm analysis as well as the use of an impedance threshold device (ITD) vs. sham device during out-of-hospital cardiac arrest.[19,20] All participating sites prospectively collected cardiac arrest epidemiological data on OHCA evaluated by its participating agencies. All agencies were required to capture CPR process data, including real-time measures of CCF and compression rate. Some sites also had the capacity to collect compression depth. During the ROC PRIMED trial, sites collected the duration of both pre-shock pause and post-shock pause up to and including the third shock. All ROC participating agencies provided data for this study.

2.2. Study sample

Patients eligible for this study included those 18 years of age and older who sustained non-traumatic OHCA with a first EMS rhythm of ventricular fibrillation or pulseless ventricular tachycardia (VF/VT) for which CPR process data for at least one shock were obtained. The initial rhythm was determined to be VF/VT if the initial automatic external defibrillator (AED) analysis advised a shock or the rhythm was interpreted as VF/VT by the initial EMS provider and a shock was provided. We excluded patients who received public access defibrillation before EMS arrival, EMS witnessed arrest and those with missing survival to hospital discharge or Utstein variable data.

2.3. Measurement

We reviewed CPR process data from all eligible resuscitations. We assessed duration of pre- and post-shock pauses, CCF, compression rate and compression depth (when available) up to and including the third shock. Following the principles of uniform reporting of measured quality of CPR described by Kramer-Johansen et al.[21] pre-shock pause was defined as the time interval between chest compression cessation (as detected in the impedance channel waveform) and shock delivery. Post-shock pause was defined as the time between shock delivery and chest compression resumption (as detected in the impedance channel waveform). Peri-shock pause was defined as the total of the pre- and post-shock pause time. CCF was defined as the proportion of time spent performing chest compressions during which the patient was without spontaneous circulation. Individual shocks with missing values for length of pauses were included as long as there was at least one non-missing pause length among the shocks considered. The primary outcome measure was survival to hospital discharge. The secondary outcome measure was neurologically intact survival to hospital discharge with Modified Rankin Score (MRS) ≤ 3.

2.4. Statistical analysis

To assess whether these cases were subject to selection bias, we used descriptive statistics to compare all VF/VT episodes in our analysis with VF/VT episodes without electrocardiogram (ECG) recordings from all participating sites. We used multivariable logistic regression models to assess the association between median shock pause duration (pre-, post- and peri-) and survival to hospital discharge. To minimize the impact of confounding by other resuscitation variables occurring later in prolonged resuscitations, these models included pause duration from only the first three shocks. Data from additional shocks (where applicable) were used in sensitivity analyses. Our model examined the shock pause length (seconds) categorically (<10, 10–20, ≥20 for pre-shock pause, <5, 5–10, ≥10 for post-shock pauses and <20, 20–40, ≥40 for peri-shock pauses). We also examined the length of pauses as a continuous variable (change presented as an increase in length by 5 s). Log-linearity of the continuous version of the variable was assessed using Lowess graphs and was found appropriate for pauses up to 40 s for pre- and post-shock pauses and for pauses up to 50 s for peri-shock pauses. We adjusted for recognized Utstein predictors of survival: age, gender, public location, bystander witnessed status, bystander CPR, time from 911 dispatch to first vehicle arrival and ROC site. We also adjusted for the CPR metrics of CCF and compression rate. We did not adjust for compression depth due to the inability of all ROC sites to collect this CPR metric. Data management was performed in S-PLUS (version 6.2.1; Insightful Corporation, Seattle, WA) while regression analysis was performed using Stata statistical software (release 11; StataCorp LP, College Station, TX).

3. Results

Fig. 1 displays a consort diagram of all patients treated during the ROC PRIMED trial as well as the cohort included ($n = 2006$)

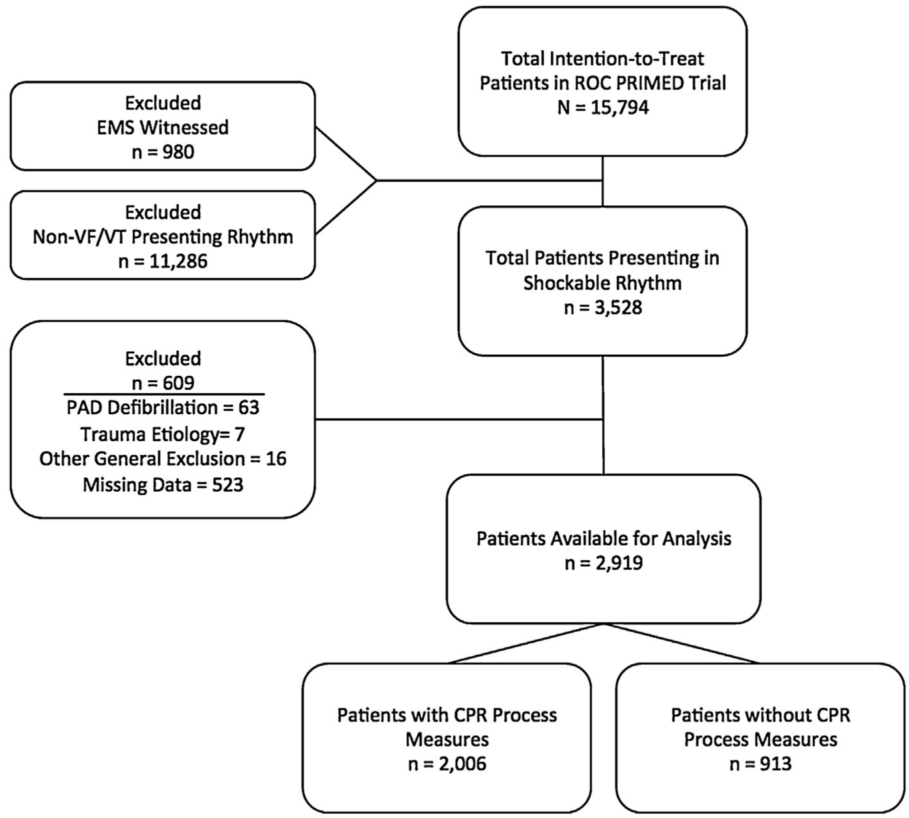

Fig. 1. Consort diagram of study cohort.

in our statistical analysis. Table 1 displays baseline characteristics for VF/VT cases included and VF/VT cases excluded (due to lack of available or interpretable ECG recordings) from the study. The study population was similar with respect to sex, witnessed status, bystander CPR, and location compared to those without CPR process measures. Median (IQR) age was lower in the study cohort 64 (54, 75) vs.70 (55, 81). Table 2 displays CPR process measures for the study population. Over a median of 9 (5, 13) minutes studied, the median (IQR) shock pause durations in the study sample were peri-shock pause 15 s (8, 22), post-shock pause 6 s (4, 9) and peri shock pause 22 s (14, 31). For each CPR quality variable we as well note the percentage of cases in which CPR metrics did not meet current AHA/ILCOR guidelines[6] (compression depth or rate) or benchmarks set by the ROC study monitoring committee (pre-, post- or peri-shock pause and CCF) during the ROC PRIMED trial.

Table 1
Patient and system characteristics comparing cases included in the analysis to those excluded due to lack of available CPR process files. CPR = cardiopulmonary resuscitation; IQR = interquartile range; VT/VF = ventricular tachycardia/ventricular fibrillation.

	Cases with CPR process data	Cases without CPR process data
n	2006	913
Median age (IQR)	64 (54, 75)	70 (55, 81)
Male, *n* (%)	1569 (78.2%)	701 (76.8%)
Public location, *n* (%)	632 (31.5%)	274 (30.0%)
Witnessed status		
Bystander, *n* (%)	1371 (68.3%)	634 (69.4%)
Unknown, *n* (%)	36 (1.8%)	13 (1.4%)
Unwitnessed, *n* (%)	599 (29.9%)	266 (29.1%)
Bystander CPR, *n* (%)	1064 (53.0%)	458 (50.2%)
Median arrival time (IQR)	5.4 (4.2, 6.8)	5.6 (4.3, 7.0)

Fig. 2 displays unadjusted data on survival to hospital discharge as a function of median shock pause length. With respect to pre-shock pause, the highest survival to hospital discharge occurred in the 10.1–15.0 s group (29.6%) with 28.9% survival for ≤15 s as compared to 20.3% for those with pre-shock pause >15 s. With respect to post-shock pause, the highest survival to hospital discharge occurred in the ≤5 second group (30.3%) compared to 20.4% for those with a post-shock pause >5 s. Regarding peri-shock pause, the highest survival to hospital discharge occurred in the

Table 2
CPR process data in study sample.

# of cases	2006
Median #available minutes w/CPR process data (IQR)	9 (5, 13)
Pre-shock pause (*n* = 4197)	
Median (IQR)	15 (8, 22)
>20 s, *n* segments (%)	1231 (29.3%)
Post-shock pause (*n* = 4396)	
Median (IQR)	6 (4, 9)
>20 s, *n* segments (%)	286 (6.5%)
Peri-shock pause (*n* = 4095)	
Median (IQR)	22 (14, 31)
>40 s, *n* segments (%)	481 (11.7%)
Chest compression fraction (*n* = 2006)	
Median (IQR)	0.71 (0.60, 0.83)
<0.60, *n* segments	500 (24.9%)
Compression depth (*n* = 1139)	
Median (IQR)	43.0 (36.6, 50.0)
<37 mm, *n* segments (%)	298 (26.2%)
Compression rate (*n* = 2006)	
Median (IQR)	110.0 (100.5, 122.5)
<80 or >120, *n* segments (%)	647 (32.3%)
Median # of shocks (IQR)	3.0 (2.0, 5.0)

CPR = cardiopulmonary resuscitation; IQR = interquartile range; *n* (pre-, post-, peri-shock pause) = number of shock pause intervals. *n* (chest compression fraction, chest compression depth, chest compression rate) = number of cases for which data was available.

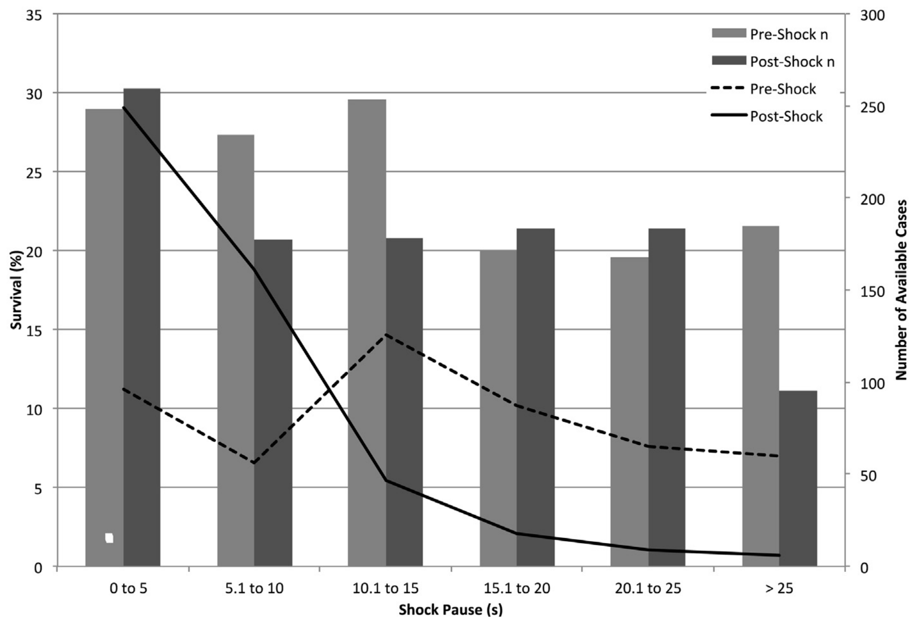

Fig. 2. Plot of unadjusted survival to hospital discharge versus median shock pause interval. Survival results are shown as column plots referring to the left-side axis, categorized into 5 shock pause interval ranges, and stratified by pre-shock and post-shock pause classification. Counts of available cases for each survival estimate are shown for each shock pause interval range as line plots referring to the right-side axis.

≤20 second group (31.7%) compared to 19.4% for those with a peri-shock pause >20 s.

Fig. I (supplemental) displays unadjusted data on survival to hospital discharge as a function of median pre- and post-shock pause duration as a continuous variable. The pre-shock pause Lowess curve demonstrates two plateaus, one extending from 0 to 10 s and a second from 25 to 40 s. The association is not linear in all segments but does decrease over time. The post-shock pause Lowess curve demonstrates a sharp decrease in survival from 0 to 5 s followed by a moderate decrease in survival from 5 to 10 s and a more pronounced decrease in survival from 10 to 50 s.

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Table 3 presents a univariable comparison of CPR process measures between survivors and non survivors. Pre-shock pause was noted to be 18% shorter in survivors than non-survivors. Post-shock and peri-shock pause in this model were noted to be 17% shorter in survivors than non-survivors. There was no apparent difference in CCF, compression rate and compression depth between the groups. Pre-, post-, and peri-shock pause durations are all significantly different ($p < 0.001$) between survivors and non-survivors while no significant difference was noted in CCF, compression rate and compression death between survivors and non-survivors.

Table 3
Univariable comparison of CPR process measures between survivors and non-survivors.

	Survivors	Non-survivors
n	490	1516
Median (IQR) pre-shock pause, s	14 (8, 21)	17 (10, 22)
Median (IQR) post-shock pause, s	5 (3.5, 8.5)	6 (5, 10)
Median (IQR) peri-shock pause, s	20 (14, 29)	24 (17, 31.5)
Median (IQR) CCF	0.70 (0.58, 0.83)	0.72 (0.60, 0.84)
Median (IQR) compression rate	110 (100.5, 121)	111 (100.4, 123)
Median (IQR) compression depth	43.7 (37.4, 49.2)	42.7 (36.2, 50.1)

CPR = cardiopulmonary resuscitation; CCF = chest compression fraction; IQR = interquartile range.

Table 4 presents unadjusted and adjusted odds ratios in a model that examined the relationship between pre-, post-, and peri-shock pause duration, and survival to hospital discharge. Median pre-shock pause was significantly associated ($p < 0.001$) with survival to hospital discharge when adjusted for median post-shock pause, mean CCF, mean compression rate, site and Utstein variables. Specifically, episodes with a median pre-shock pause <10 s had a higher odds of survival to hospital discharge (OR: 1.52, 95% CI: 1.09, 2.11) when compared to episodes with a median pre-shock pause ≥20 s. Median peri-shock pause was as well significantly associated ($p < 0.001$) with survival to hospital discharge when adjusted for mean CCF, mean compression rate, site and Utstein variables. Episodes with a median peri-shock pause <20 s had a higher odds of survival to hospital discharge (OR: 1.82, 95% CI: 1.17, 2.85) when compared to episodes with a median peri-shock pause ≥40 s. Age, public location, bystander witnessed status, site, log response time (all $p < 0.001$) and bystander CPR ($p < 0.02$) were all significantly associated with survival to hospital discharge. In the same model, post-shock pause (OR: 1.34, 95% CI: 0.94, 1.90) was not associated with survival to hospital discharge.

In a separate model exploring the relationship between shock pause duration and neurologically intact survival with MRS ≤ 3, pre- and peri-shock pause were significantly associated ($p < 0.001$) with positive neurological outcome. Specifically, the odds of neurologically intact survival were significantly higher with pre-shock pause <10 s (OR: 1.49, 95% CI: 1.05, 2.13) and peri-shock pause <20 s (OR: 1.99, 95% CI: 1.21, 3.29) compared to episodes with pre-shock pause ≥20 s and peri-shock pause ≥ 40 s.

When modeled continuously, odds of survival were 7% lower (OR: 0.93; 95% CI: 0.87, 0.99) for every 5-s difference in pre-shock pause and 6% lower (OR: 0.94; 95% CI: 0.90, 0.99) for every 5-s difference in peri-shock pause. No significant association was found between post-shock pause (OR: 0.95; 95% CI: 0.86, 1.04) and survival in this model.

4. Discussion

To the best of our knowledge, this study represents the largest out-of-hospital study to date examining the relationship between

Table 4
Logistic regression analysis demonstrating unadjusted and adjusted estimates[a] evaluating the association between shock pause duration (seconds) and survival to hospital discharge.

	Pre and post shock pause			
	Unadjusted OR	95% CI	Adjusted OR	95% CI
Median pre-shock ≥ 20	Reference		Reference	–
Median pre-shock 10–19.9	1.34	(1.09, 1.66)	1.25	(0.95, 1.65)
Median pre-shock <10	1.73	(1.36, 2.19)	1.52	(1.09, 2.11)
Median post-shock ≥ 10	Reference		Reference	–
Median post-shock 5–9.9	1.09	(0.86, 1.37)	1.02	(0.75, 1.38)
Median post-shock <5	2.01	(1.58, 2.55)	1.34	(0.94, 1.90)
Median peri-shock ≥ 40	Reference		Reference	
Median peri-shock 20–39.9	1.22	(0.88, 1.71)	1.16	(0.76, 1.76)
Median peri-shock <20	2.17	(1.56, 3.02)	1.82	(1.17, 2.85)

CI = confidence interval; CPR = cardiopulmonary resuscitation.

[a] Estimates adjusted for mean chest compression fraction, mean chest compression rate, site and Utstein (age, gender, public location, bystander witnessed status, bystander CPR, log response time) variables.

peri-shock pause and survival to hospital discharge from shockable cardiac arrest. We have confirmed previous work on peri-shock pauses, further strengthening the conclusion that peri-shock pauses <20 s in the early resuscitation period are strongly associated (OR: 1.82, 95% CI: 1.17, 2.85) with survival to discharge when compared to episodes with peri-shock pause ≥40 s. The benefit to survival by lowering peri-shock pause appears to be driven almost exclusively by the pre-shock pause length where we noted improved survival for episodes with pre-shock pauses <10 s compared to episodes in which pre-shock pause was ≥20 s (OR: 1.51, 95% CI: 1.09, 2.11). As in our previous study, we found no significant association between post-shock pause and survival to hospital discharge.

These peri-shock pause findings are consistent with our findings employing the Consortium's cardiac arrest registry database (Epistry)[17] as well as previously published data that relate pre-shock pause to return of spontaneous circulation (ROSC). Edelson et al.[9] demonstrated a relationship between termination of ventricular fibrillation (VF) and shorter pre-shock pause intervals in a study of cardiac arrest in both the hospital and out-of-hospital settings. Sell et al.[22] determined a similar relationship between pre- and post-shock pauses and the likelihood of ROSC in patients presenting in VF in a small study of patients suffering from OHCA. Our median pre-shock pause interval of 15 s was slightly lower than our value using the Epistry database (15.6 s) and consistent with that demonstrated by Kramer-Johansen[23] (15 s) and Vadeboncoeur (14.5 s).[24]

Significant site variation in median pre-shock pause length (data not shown) was noted in our study. Several factors may explain this variation. During the PRIMED trial, use of defibrillators in AED mode was common, resulting in prolonged pre-shock pauses required for the defibrillator charging phase. This prolongation of pre-shock pause in automatic defibrillator mode has been demonstrated previously.[12,25] Interestingly, sites with the lowest pre-shock pauses tended to employ techniques and defibrillator technology known to decrease pre-shock pause. "Compressions during charging", a technique whereby the rescuer provides chest compressions during the defibrillator charging phase, has been shown to decrease pre-shock pause in AED mode. Edelson et al.[26] have recently shown that rescuer performance of chest compressions during the defibrillator "charging phase" significantly lowered pre-shock pause intervals to less than 3 s (median 2.6 s; IQR: 1.9, 3.8). Similar results can be obtained by pre-charging the manual mode defibrillator (pressing the defibrillator charge button prior to completion of the CPR cycle) thereby eliminating the defibrillator charge time after rhythm assessment decreasing pre-shock pause.[27]

Technological advances in defibrillator software which allows underlying rhythm analysis during CPR as well as battery charging and delivery of a shock immediately at the end of the CPR interval could significantly decrease pre-shock pause intervals.[28,29] Similarly, improved algorithms allowing for earlier detection of shockable rhythms while working in automated mode could also decrease pre-shock pause time. Although the "optimal" pre-shock pause interval of 3 s noted by Sell et al.[22] were rarely noted in ROC PRIMED patients, it is clear that some sites within the consortium are closing in on these values. Given these findings, a decrease to a consistent median pre-shock pause of <10 s and peri-shock pause <20 s across the consortium appears realistic carrying with it a significant opportunity to improve resuscitation outcomes.

Our current study replicates the findings of our earlier work regarding post-shock pause with no significant association noted between post-shock pause interval and survival. Experimental studies and human observational studies[30–33] have noted survival benefits when there were large reductions in post-shock pause as occurs with a single shock versus stacked shock protocol. Whether additional reduction in the post-shock interruption using a single-shock approach would affect survival is uncertain based on the current results. Indeed a shorter post-shock interruption was significantly associated with a greater likelihood of survival in unadjusted models. Following adjustment, post shock pause <5 s had a 34% greater odds of survival though this association was not statistically significant. One clinical explanation is that shorter post-shock pause may be helpful in some but may have an adverse effect in others where early initiation of post-shock compressions may trigger re-fibrillation as noted in work by Berdowksi et al.,[34] Further study is required to better understand the optimal post-shock pause interval and its relationship to resuscitation success.

Our study has several limitations. We attempted to control for confounding by including important predictor variables in our logistic regression model. We did not include analyze early or analyze late arm or ITD use as a variable in our regression model as neither variable was shown to be predictive of survival during the ROC PRIMED study. Although our data is taken from a randomized controlled trial, the findings are observational, and as such we can only demonstrate an association between peri-shock pause and survival to hospital discharge rather than a causal relationship. A randomized trial would be required to evaluate a causal relationship but may not be feasible given our current findings. Our regression model did not control for compression depth due to the large number of sites unable to collect this metric during the trial (56% missing rate of compression depth data). Missing shock pause data is not uncommon when using impedance channel measurement of CPR process. Our rate of missing shock pause data during this study was 11% (13% pre-shock and 9% post-shock), a marked improvement compared to 26% in our Epistry paper.[14] Given the large number of shock pause intervals reviewed in this study and the similarity between those included in the study and those excluded due to missing shock pause data, it would be unlikely that our results would have been significantly impacted by this limitation. Lastly, the study took place in regions with high performing and heavily monitored EMS systems with rapid response times and overall high CPR quality. As such it is uncertain as to the applicability of our findings to other EMS systems without similar system response optimization and CPR quality characteristics.

5. Conclusion

In patients with cardiac arrest presenting in a shockable rhythm during the ROC PRIMED trial, pre-shock pauses <10 s and peri-shock pauses <20 s were significantly associated with higher odds of survival to both hospital discharge and neurologically intact (MRS ≤ 3) survival. Future cardiopulmonary education and technology should focus on minimizing all pre-shock pauses.

Conflict of interest statement

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