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Clinical paper

Chest compression fraction: A time dependent variable of survival in shockable out-of-hospital cardiac arrest☆

Sheldon Cheskes[a,*], Robert H. Schmicker[b], Tom Rea[b], Judy Powell[b], Ian R. Drennan[a], Peter Kudenchuk[b], Christian Vaillancourt[d], William Conway[e], Ian Stiell[d], Dion Stub[g], Dan Davis[f], Noah Alexander[c], Jim Christenson[c], the Resuscitation Outcomes Consortium (ROC) investigators

[a] University of Toronto, Toronto, ON, Canada
[b] University of Washington, Seattle, WA, United States
[c] University of British Columbia, Vancouver, BC, Canada
[d] University of Ottawa, Ottawa, ON, Canada
[e] Oregon Health and Science University, Portland, OR, United States
[f] University of California/San Diego, San Diego, CA, United States
[g] St. Paul's Hospital, Vancouver, BC, Canada

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ABSTRACT

Introduction: The role of chest compression fraction (CCF) in resuscitation of shockable out-of-hospital cardiac arrest (OHCA) is uncertain. We evaluated the relationship between CCF and clinical outcomes in a secondary analysis of the Resuscitation Outcomes Consortium PRIMED trial.

Methods: We included patients presenting in a shockable rhythm who suffered OHCA prior to EMS arrival. Multivariable logistic regression was used to determine the relationship between CCF and survival to hospital discharge, return of spontaneous circulation (ROSC), and neurologically intact survival. We also performed a secondary analysis restricted to patients *without* ROSC in the first 10 min of EMS resuscitation.

Results: Among the 2011 patients, median (IQR) age was 65 (54, 75) years, 78.2% were male, and mean (SD) CCF was 0.71 (0.14). Compared to the reference group (CCF < 0.60), the odds ratio (OR) for survival was 0.49 (95%CI: 0.36, 0.68) for CCF 0.60–0.79 and 0.30 (95%CI: 0.20, 0.44) for CCF ≥ 0.80. Results were similar for outcomes of ROSC and neurologically intact survival. Conversely, when restricted to the cohort who did not achieve ROSC during the first 10 min ($n = 1633$), compared to the reference group (CCF < 0.60), the OR for survival was 0.79 (95%CI: 0.53, 1.18) for CCF 0.60–0.79 and OR 0.88 (95%CI: 0.56, 1.36) for CCF ≥ 0.80.

Conclusions: In this study of OHCA patients presenting in a shockable rhythm, CCF was paradoxically associated with lower odds of survival. CCF is a complex measure and taken by itself may not be a consistent predictor of good clinical outcomes.

1. Introduction

Improving survival from out-of-hospital cardiac arrest (OHCA) continues to be a primary goal for Emergency Medical Services (EMS) systems worldwide.[1–3] With an annual worldwide incidence of greater than 6 million cardiac arrests[4] the search continues for the components of resuscitation essential to improve survival. With the advent of the 2010 American Heart Association-International Liaison Committee on Resuscitation (AHA-ILCOR) guidelines for Cardiopulmonary Resuscitation (CPR), interest has focused on improving survival through improvements in the characteristic components of cardiopulmonary resuscitation (CPR).[5,6]

Interruptions in chest compressions during CPR have a deleterious impact on coronary and cerebral perfusion during animal models of cardiac resuscitation.[7,8] Chest compression fraction (CCF), the proportion of time performing chest compressions during cardiac arrest has been identified as a key CPR quality performance benchmark. To maximize perfusion during chest

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* Corresponding author. Sunnybrook Centre for Prehospital Medicine, 77 Brown's Line, Suite 100. Toronto, ON, Canada M8 W 3S2. Tel.: +(416) 667-2200; fax: +1 416 667 9776.
E-mail address: Sheldon.Cheskes@sunnybrook.ca (S. Cheskes).

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compressions, a CPR fraction of 80% or greater has been recommended in a variety of settings.[9] However, previous observational studies in human resuscitation have yielded inconsistent results with respect to survival from OHCA when CCF is employed as an independent predictor variable.[10–12] CCF may play a role in predicting survival from OHCA when resuscitation length is prolonged and high quality CPR is being performed.[13] Prior studies however have been limited by single site experiences, lack information about potential confounding variables such as interval to return of spontaneous circulation (ROSC) or duration of resuscitations.

To evaluate the prognostic role of CCF, we performed a secondary analysis of the Prehospital Resuscitation using an Impedance Valve and Early vs. Delayed Analysis Randomized Controlled trial known as ROC PRIMED.[14] The objective of this study was to assess the relationship between CCF and clinical outcomes from shockable OHCA during the ROC PRIMED randomized controlled trial. We hypothesized that greater CCF would be associated with better clinical outcomes.

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.[15] From June 2007-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.[16] The trial studied two different resuscitation strategies, a 30 s vs. a 3 min CPR strategy prior to rhythm analysis as well as the use of an impedance threshold device (ITD) vs. sham device during OHCA.[17–19] All participating sites prospectively collected cardiac arrest epidemiological data on OHCA evaluated by its participating agencies. All agencies were required to capture electronic defibrillator CPR process data, including real-time measures of CCF, compression depth (not available on all defibrillators), compression rate and shock pause duration (up to the third shock abstracted from defibrillator files). All ROC participating agencies provided data for this study. The ROC PRIMED protocol was approved by the institutional review or research ethics boards at each participating site.[14] The trial was conducted under waiver of informed consent with community engagement consistent with ROC cardiac arrest interventional studies.

2.2. Study sample

Patients eligible included those greater than 18 years of age 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 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 or those who were missing survival to hospital discharge or Utstein variable data.

2.3. CPR measurement

We reviewed CPR process data from all eligible resuscitations. We assessed duration of pre- and post-shock pauses, CCF, compression depth and compression rate. CCF was defined as the proportion of time spent performing chest compressions during CPR. We analyzed data from all available defibrillator files from the time of first available documented EMS compression to the time of first ROSC or a minimum of 10 min after first documented EMS compression (first 5 min of CPR process data plus first 5 min after advanced airway management). Sites had the option of entering more than the minimum amount of CPR quality data if available. ROSC was defined in the ROC PRIMED manual of operations (MOO) as the documented presence of a measurable pulse and blood pressure at any time after initiation of resuscitative efforts with no minimum duration of ROSC.[20]

2.4. Outcomes

Our primary outcome measure was to assess the relationship between CCF and survival to hospital discharge. Our secondary outcome measure was to assess the relationship between CCF and neurologically intact survival with Modified Rankin Score (MRS) ≤ 3.

2.5. 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. Because the duration of resuscitation is a potential confounder of CCF and clinical outcome,[13] we examined patient characteristics and CPR process measurements by resuscitation length and timing of ROSC (ROSC <5 min, ROSC between 5 and 10 min, no ROSC <10 min). Unadjusted survival rates were examined by CCF category (0% to 59%, 60% to 79%, and 80% to 100%) based on the mean CCF delivered to the patient over the minutes of available data beginning with the first documented chest compression. We constructed multiple logistic regression models to estimate the adjusted odds ratio of survival for each category of CCF relative to the lowest category (0% to 59%). We adjusted for recognized Utstein predictors of survival: age (continuous), sex (male; female), arrest location (private; public), witness status (not witnessed; bystander witnessed; unknown), bystander CPR (yes; no), time from 911 dispatch to first vehicle arrival (continuous), ROC site and the CPR quality metrics of compression rate (80–120; <80 or >120) and shock pause duration (<10; 10–20, >20 s). We were unable to adjust for compression depth as it was not able to be collected on all defibrillators used in the ROC PRIMED study. As such, compression depth was only available in 1140 (57%) cases and was excluded from our regression models.

Several post hoc analyses were performed. To account for the length of resuscitation and timing of ROSC, similar logistic regression models were used to examine the association between CCF and survival to hospital discharge in each of the three subgroups—ROSC <5 min, ROSC between 5 and 10 min, no ROSC <10 min. We also assessed the prognostic role of CCF in cases with ROSC and a minimum of 20 min of documented CPR data.[13] In this analysis, CCF was categorized dichotomously according to the median length of resuscitation. We adjusted for age, sex, EMS response interval, witness status and bystander CPR.

Pearson chi-square test was used to assess goodness of fit. Variance inflation factor (VIF) was used to assess for multicollinearity between CPR quality metrics. Data management was performed in S-PLUS (version 6.2.1), c (2003), Insightful Corporation, Seattle, WA. R Regression analyses were performed in StataCorp. 2009. *Stata Statistical Software*: *Release 11*. College Station, TX: StataCorp LP.

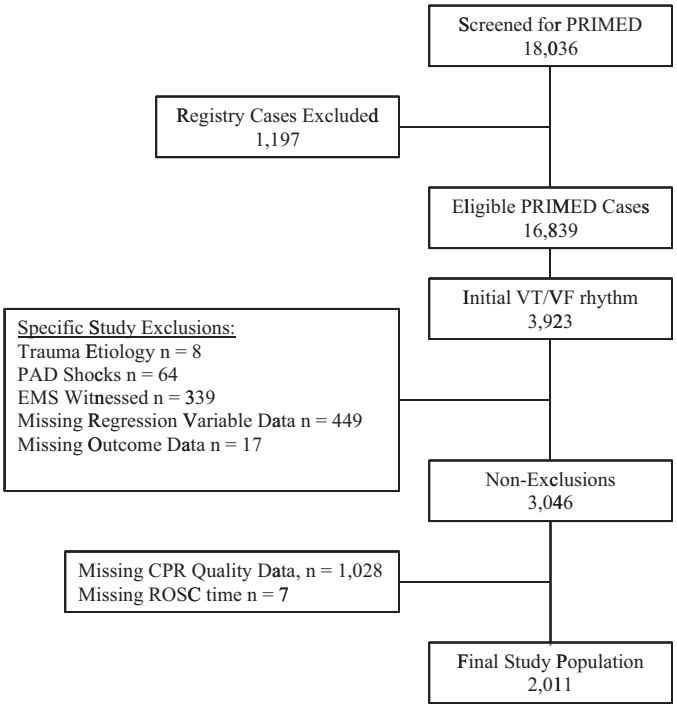

Fig. 1. CONSORT diagram of study population.

3. Results

Fig. 1 displays a CONSORT diagram of the study population. The initial population consisted of all ROC PRIMED cases. Excluded from the ROC PRIMED trial were cases with no ITD opened and either a general trial exclusion, a non-fire/EMS rhythm analysis or a non-ROC agency on scene that had started CPR ($n = 1197$). We then excluded cases with non-VT/VF initial rhythm ($n = 12{,}916$), leaving 3923 PRIMED cases presenting with a shockable rhythm. Specific study exclusions included cases with PAD shocks ($n = 64$), cases with traumatic etiology ($n = 8$), EMS witnessed cases ($N = 339$), cases missing regression variable data ($n = 449$) or outcome data ($n = 17$). Of the 3046 eligible PRIMED cases, 1035 cases (34%) were excluded because of incomplete CPR process data or lack of time of ROSC, leaving 2011 cases available for the current study.

Table 1 displays baseline characteristics for VF/VT cases included and VF/VT cases excluded (due to lack of available CPR quality data or time of ROSC) from the study. The study population was similar to the excluded population with respect to all Utstein variables. When assessing the time of ROSC between the two groups a greater proportion of patients with ROSC < 5 min was noted in the excluded sample.

Table 2 displays patient characteristics by length of resuscitation and timing of ROSC. Overall median (IQR) age was 64 years (54, 75) while 78.2% were male. Two-thirds of patients had their arrest witnessed by a bystander (67.5%) while over half had bystander CPR performed (53.3%). The proportion with bystander witnessed arrests, bystander CPR, and public location were highest in the early ROSC group compared to late or no ROSC < 10 min group. Similarly median (IQR) EMS arrival time and ALS arrival time was shortest amongst the early ROSC group although the presence of ALS on scene did not differ amongst the three cohorts.

The study reviewed a total of 18,336 min (IQR 5–12 min per individual case) of CPR process measures among the 2011 cases, comprising 33.8% of the total duration of resuscitation. The mean (SD) number of CPR process measures minutes per resuscitation was 9.1 (5.0). CPR quality process measures by length of resuscitation and timing of ROSC can be viewed in Table 3. Mean (SD) CCF was 0.71 (0.14) and mean (SD) compression rate was 111.3 (16.7). CCF increased with length of resuscitation ($p < 0.01$). Mean (SD) pre-shock pause was 16.9 s (10.4) and mean (SD) post-shock pause was 8.5 s (7.9) with no significant change over the length of the resuscitation.

Table 1
Patient and system characteristics comparing cases included in the analysis to those excluded due to lack of available CPR process data or time of ROSC.

	VF/VT included	VF/VT excluded
n	2011	1035
Median age (IQR)	64 (54, 75)	64 (54, 76)
Male, *n* (%)	1572 (78.2%)	796 (76.9%)
Public location, *n* (%)	626 (31.1%)	311 (30.0%)
Witnessed status		
EMS, *n* (%)	0 (0.0%)	0 (0.0%)
Bystander, *n* (%)	1358 (67.5%)	722 (57.1%)
Unknown, *n* (%)	38 (1.9%)	16 (1.3%)
None, *n* (%)	615 (30.6%)	297 (23.5%)
Bystander CPR, *n* (%)	1072 (53.3%)	517 (50.0%)
Median arrival time (IQR)	5.4 (4.1, 6.8)	5.5 (4.3, 7.0)
ALS on scene, *n* (%)	1946 (96.8%)	1011 (97.7%)
No ROSC	943 (46.9%)	519 (50.1%)
ROSC within 5 min	84 (4.2%)	78 (7.5%)
ROSC within 5–10 min	262 (13.0%)	111 (10.7%)
ROSC after 10 min	722 (35.9%)	308 (30.0%)
Missing time to ROSC	0 (0.0%)	19 (1.8%)

VF = ventricular fibrillation VT, VT = ventricular tachycardia, IQR = interquartile range, EMS = emergency medical services, CPR = cardiopulmonary resuscitation, ALS = advanced life support, ROSC = return of spontaneous circulation

Table 4 displays unadjusted outcome rates by mean CCF. Survival to hospital discharge for CCF groups 0–0.60, 0.61–0.80 and 0.81–1.00 were 29.8%, 23.8% and 21.6% respectively. Trends were similar for ROSC at ED and MRS ≤ 3. Interestingly, the trend of improved survival in the lowest CCF category was not noted in the subgroup of patients with no ROSC prior to 10 min with similar rates of survival in all three categories of CCF.

Table 5 displays regression estimates for the overall population and all three ROSC subgroups. After adjustment for known confounders the Odds Ratio (OR) (95% CI) of survival to hospital discharge for those with CCF ≥ 0.80 compared to CCF < 0.60 was 0.30 (0.20, 0.44) while the OR (95% CI) of survival for episodes with CCF 0.60–0.79 compared to CCF < 0.60 was 0.49 (0.36, 0.68). Within the model, pre-shock pause <10 s, younger age, quicker EMS arrival time, witness status, bystander CPR, public location and ROC site were all significantly associated with patient survival ($p < 0.05$). Within the no ROSC prior to 10 min of resuscitation subgroup, the association was not statistically significant. Compared to the CCF < 0.60, the OR (95% CI) of survival was 0.88 (0.56, 1.38) for cases with CCF ≥ 0.80 and 0.79 (0.53, 1.18) for cases with CCF 0.60–0.79. All covariates in the study population remained significant in the no ROSC prior to 10 min model except for bystander CPR 1.32 (0.99, 1.76). Models examining the association between CCF and the clinical outcomes of ROSC and neurological function (MRS ≤ 3) were similar in result and can be reviewed in Supplementary Table 1.

In a post hoc analysis of cases with ROSC and >20 min of resuscitation ($n = 288$), there was no significant association between survival to hospital discharge and CCF for those with an average CCF greater than or equal to the median (0.82) compared to those with an average CCF lower than the median, OR = 0.89, 95% CI (0.37, 21.5) after adjusting for age, sex, arrival time, bystander witnessed and presence of bystander CPR. We did not adjust for site in this analysis.

Pearson chi-square test was used to confirm the goodness of fit of our regression models ($p = 0.26$). As well testing for multicollinearity of CPR quality metrics yielded a VIF < 10 suggesting no colinearity between CPR quality metrics.

Table 2
Patient characteristics of Study Population.

	Screened shockable rhythm (primary analysis)	ROSC within 5 min	ROSC between 5–10 min	No ROSC prior to 10 min
n	2011	84	262	1665
Median age (IQR)	64 (54, 75)	61 (51, 71)	63 (53, 75)	65 (54, 76)
Male, *n* (%)	1572 (78.2%)	67 (79.8%)	190 (72.5%)	1315 (79.0%)
Public location, *n* (%)	626 (31.1%)	42 (50.0%)	96 (36.6%)	488 (29.3%)
Witnessed status				
Bystander, *n* (%)	1358 (67.5%)	71 (84.5%)	206 (78.6%)	1081 (64.9%)
None, *n* (%)	615 (30.6%)	11 (13.1%)	52 (19.8%)	552 (33.2%)
Unknown, *n* (%)	38 (1.9%)	2 (2.4%)	4 (1.5%)	32 (1.9%)
Bystander CPR, *n* (%)	1072 (53.3%)	59 (70.2%)	152 (58.0%)	861 (51.7%)
Median arrival time (IQR)	5.4 (4.1, 6.8)	4.6 (3.8, 6.0)	5.0 (4.0, 6.5)	5.5 (4.2, 6.9)
ALS on scene, *n* (%)	1946 (96.8%)	83 (98.8%)	255 (97.3%)	1608 (96.6%)
Median ALS arrival time (IQR)	7.9 (5.6, 11.0)	6.9 (4.4, 9.2)	7.4 (5.0, 11.0)	7.9 (5.5, 11.0)

ROSC = return of spontaneous circulation, IQR = interquartile range, CPR = cardiopulmonary resuscitation, ALS = advanced life support.

Table 3
CPR process data of Study Population.

	Screened shockable rhythm	ROSC within 5 min	ROSC between 5-10 min	No ROSC prior to 10 min
No. of cases	2011	84	262	1665
Mean no. available minutes w/CPR process data (SD)	9.1 (5.0)	2.8 (1.0)	5.7 (1.8)	10.0 (5.0)
Minutes from call to dispatch to CPR start, median (IQR)	7.8 (6.2, 9.4)	7.5 (5.9, 9.1)	7.4 (6.0, 9.0)	7.8 (6.3, 9.6)
Minutes from CPR start to Defib pads on, median (IQR)	0.6 (0.0, 1.3)	0.4 (0.0, 1.0)	0.4 (0.0, 1.1)	0.6 (0.0, 1.3)
Mean CCF (SD)				
All Minutes	0.71 (0.14)	0.66 (0.17)	0.69 (0.14)	0.71 (0.14)
Minutes 0–5	0.69 (0.16)	0.66 (0.17)	0.68 (0.15)	0.69 (0.15)
Minutes 5–10	0.71 (0.19)	–	0.71 (0.20)	0.71 (0.19)
Minutes 10+	0.74 (0.18)	–	–	0.74 (0.18)
Mean compression rate (SD)				
All Minutes	111.3 (16.7)	108.2 (18.2)	109.3 (15.8)	111.7 (16.7)
Minutes 0–5	110.3 (18.6)	108.2 (18.2)	108.4 (16.9)	110.7 (18.9)
Minutes 5–10	112.0 (19.1)	–	113.6 (16.7)	111.8 (20.2)
Minutes 10+	114.2 (18.6)	–	–	114.2 (18.6)
Pre-shock pause				
Mean (SD)	16.9 (10.4)	14.7 (9.0)	16.9 (13.9)	17.0 (10.2)
>20 s, *n* segments (%)	1219 (29.1%)	29 (23.8%)	118 (24.1%)	1072 (87.9%)
Post-shock pause				
Mean (SD)	8.5 (7.9)	8.0 (8.7)	7.8 (11.6)	8.6 (7.8)
>20 s, *n* segments (%)	276 (6.3%)	4 (3.3%)	28 (5.5%)	244 (88.4%)
Peri-shock pause				
Mean (SD)	25.2 (14.0)	22.2 (13.0)	24.8 (20.5)	25.4 (13.7)
>40 s, *n* segments (%)	463 (11.3%)	11 (9.6%)	48 (10.1%)	404 (87.3%)

ROSC = return of spontaneous circulation, CCF = chest compression fraction, SD = standard deviation, IQR = interquartile range.

4. Discussion

In this multi-center secondary analysis of CPR quality data from the ROC PRIMED study we observed a paradoxical significant lower survival among shockable OHCA associated with CCF > 0.6. Our regression models stratifying for timing of ROSC as well as length of resuscitation and adjusted for the Utstein variables and CPR quality metrics of shock pause duration and chest compression rate failed to demonstrate an improvement in survival with increasing CCF. In an attempt to control for confounding by cases with early ROSC we found no significant relationship between CCF and survival for cases without ROSC in the first 10 min of resuscitation. Given the small number of cases with CCF 0–0.4, ($n = 55$) we adjusted our reference range in our regression models to CCF between 0.4 and 0.6 ($n = 314$) and noted no change in our point estimates. Including only cases with compression depth ($n = 1140$) as a variable in our regression model as well as those patients undergoing percutaneous coronary intervention did not impact our study findings. Compression depth of >37 mm was not associated with improved outcomes in this model OR 95% CI 1.17 (0.80, 1.71) which appears contrary to previous studies demonstrating a positive association between compression depth and survival.[12,21] Perhaps as shown by Sugarman et al.[22] provider fatigue may occur during resuscitations where CCF is increased which may have a detrimental impact on compression depth. We performed a post hoc analysis assessing the potential confounding impact of an interaction between

Table 4
Unadjusted survival to hospital discharge by mean chest compression fraction and ROSC subgroup.

Mean chest compression fraction	Screened shockable rhythm	ROSC within 5 min	ROSC between 5 and 10 min	No ROSC prior to 10 min
0–0.60, Outcome *n* (%)	110 (29.8%)	18 (81.8%)	44 (73.3%)	48 (16.7%)
0.61–0.80, Outcome *n* (%)	258 (23.8%)	39 (81.3%)	92 (63.9%)	127 (14.2%)
0.81–1.00, Outcome *n* (%)	120 (21.6%)	9 (64.3%)	31 (53.4%)	80 (16.5%)

ROSC = return of spontaneous circulation.

Table 5
Multivariable logistic regression analysis of study population demonstrating adjusted odds ratios for survival to hospital discharge in each ROSC subgroup.

Model	Screened shockable rhythm	ROSC within 5 min	ROSC between 5 and 10 min	No ROSC prior to 10 min
N	2011	84	262	1665
CCF < 0.60	Reference	Reference	Reference	Reference
CCF 0.60–0.79	0.49 (0.36, 0.68)	0.39 (0.07, 2.09)	0.47 (0.20, 1.07)	0.79 (0.53, 1.18)
CCF ≥ 0.80	0.30 (0.20, 0.44)	0.24 (0.02, 2.38)	0.25 (0.09, 0.73)	0.88 (0.56, 1.38)
Pre-shock pause <10 s	1.82 (1.29, 2.57)	6.74 (0.92, 49.4)	2.19 (0.92, 5.19)	1.59 (1.07, 2.35)
Pre-shock pause 10–20 s	1.15 (0.87, 1.52)	4.28 (0.87, 21.2)	1.91 (0.90, 4.03)	1.08 (0.78, 1.51)
Pre-shock pause >20 s	Reference	Reference	Reference	Reference
Post-shock pause <10 s	1.38 (0.80, 2.37)	1.05 (0.04, 27.9)	4.08 (0.88, 18.9)	1.58 (0.83, 3.03)
Post-shock pause 10–20 s	1.20 (0.68, 2.12)	0.37 (0.01, 9.81)	1.72 (0.36, 8.27)	1.10 (0.55, 2.22)
Post-shock pause >20 s	Reference	Reference	Reference	Reference
Comp rate 80–120	0.92 (0.70, 1.21)	0.41 (0.08, 2.14)	0.91 (0.45, 1.83)	0.76 (0.55, 1.06)
Comp rate <80 or >120	Reference	Reference	Reference	Reference
Age	0.97 (0.96, 0.98)	0.91 (0.86, 0.98)	0.94 (0.92, 0.96)	0.97 (0.96, 0.98)
Male	1.21 (0.92, 1.59)	3.87 (0.51, 29.73)	0.94 (0.47, 1.86)	1.08 (0.76, 1.53)
Arrival time	0.85 (0.80, 0.91)	0.82 (0.57, 1.17)	0.94 (0.82, 1.07)	0.81 (0.75, 0.87)
Not witnessed	Reference	Reference	Reference	Reference
Bystander witnessed	2.75 (2.07, 3.64)	6.33 (0.90, 44.8)	1.84 (0.88, 3.82)	2.18 (1.56, 3.05)
Unknown witnessed	0.84 (0.29, 2.40)	Dropped	0.71 (0.07, 7.01)	Dropped
No Bystander CPR	Reference	Reference	Reference	Reference
Bystander CPR	1.29 (1.02, 1.63)	2.41 (0.47, 12.4)	1.42 (0.76, 2.66)	1.32 (0.99, 1.76)
Public location	1.60 (1.26, 2.04)	0.40 (0.09, 1.82)	1.65 (0.84, 3.22)	1.48 (1.10, 1.99)

CCF = Chest compression fraction, ROSC = return of spontaneous circulation.

compression depth and CCF and found the interaction term to be non-significant. The findings were consistent when assessing the relationship between CCF and the clinical outcomes of ROSC and neurologically intact survival (MRS ≤ 3) as well as our analysis of cases with ROSC and a minimum of 20 min of CPR quality data.

Given the abundance of animal data on the impact of chest compression interruptions on cerebral and coronary perfusion it would seem that our results lack biologic plausibility.[7,8,23–25] Is it possible that patients who receive poor quality CPR as measured by CCF < 0.60 may actually in some circumstance have higher rates of survival? Can CCF predict survival from shockable OHCA over the duration of resuscitation regardless of timing of defibrillation or ROSC? Our findings suggest that perhaps CCF is a time dependent variable in OHCA with a greater beneficial impact on survival during lengthy resuscitations requiring prolonged CPR to maintain cerebral and coronary perfusion. Shorter resuscitations where providers are performing multiple tasks including early defibrillation may achieve survival with paradoxically lower CCF due to multiple interruptions in CPR which often occur early in resuscitations. This observation is consistent with the gradual improvement in CCF over time noted in our study findings. The importance of our findings in the context of real world, out-of-hospital resuscitation deserve special mention. Providers beginning cardiac arrest care have no way of knowing whether resuscitation is going to be short or long, successful or unsuccessful. As such it is important that the high quality CPR be performed (including a focus on greater CPR fraction) from the outset of a resuscitation as we continue to search for the ultimate CPR quality metric or combination of metrics to allow us to more accurately predict outcomes from OHCA.

Our findings at first glance would appear to conflict with those of previously published research performed by Christenson et al.[10] employing data from the ROC Epistry data set,[15] where we found adjusted odds ratios favoring survival in the categories with the highest CCF compared with the lowest category of CCF. We would caution direct comparison of these results, as significant methodological and population differences between the two make such a comparison challenging. A significant methodological difference between the two papers is the amount of CPR quality data employed for each analysis. Our earlier research analyzed CCF data up to and including the minute of the first analysis [mean (IQR) minutes, 1.6 (1.1)] whereas our current study employs CPR quality data potentially including the full duration with a mean (IQR) of 10.5 (5.2) min. We performed a sensitivity analysis on the PRIMED data set, using CCF data up to and including the minute of the first analysis with no difference in our study findings. Second, our current analysis occurred in the setting of a randomized controlled trial in which one arm of the trial altered the duration of "up front CPR" between 30 s and 3 min as well as the use of an impedance threshold device (ITD) vs. sham device during resuscitation. In our analysis neither use of ITD or amount of "up front CPR" impacted our study findings. Finally, the population providing data for our earlier study was primarily from British Columbia and Seattle, Washington (79%) whereas this study is more representative of the multiple sites in the ROC.

The strengths of the current study are the inclusion of nearly four times the number of patients (2011 vs. 506) as well as broader participation from all ROC sites. Perhaps one of the most remarkable observations of the current data set is the marked improvement in CCF between the two studies across the consortium, a time period during which there was an important improvement in survival across the ROC consortium among shockable rhythm arrests.[26] The mean CCF increased by nearly 8% during ROC PRIMED (0.65 to 0.70) with a median CCF of 0.75. Exploring more closely cases with CCF < 0.4 decreased from 34% in our previous work to 2.7% in our current study necessitating a change in the reference ranges employed for our current study owing to the small number of patients with CCF between 0 and 0.2 ($n = 11$) as well as 0.2–0.4 ($n = 44$). This global increase in CCF across the consortium may have had the effect of minimizing any large differences in outcome related to CCF that may have been apparent prior to the ROC PRIMED trial. In other words survivors and non survivors both received high quality CPR as measured by CCF. Finally, bystander CPR was found to be a significant predictor of survival in our current study as opposed to our original work. One could postulate that perhaps higher quality bystander CPR occurred during the ROC PRIMED trial yielding patients who were more likely to benefit from early defibrillation. As well, we did note in our excluded population a higher rate of ROSC which may be explained by the occurrence of ROSC prior to or simultaneous with provider application of pads measuring CPR quality data supporting the hypothesis of high quality bystander CPR. Ultimately significant differences exist between the two data sets making direct comparison difficult.

Our current findings appear to mirror recent work by Stolz et al.[27] who studied the impact of a variety of CPR quality measures

on survival and neurological outcome from OHCA. Multivariable logistic regression was used to study CPR quality metrics and their independent association with survival to hospital discharge. Of 484 consecutive patients studied there was no significant differences noted between survivors and non survivors with regard to CCF (75.2 survivors, 76.4 non survivors). Separate regression analysis depicted no significant associations between survival and CCF. Similarly Vadeboncoeur et al.[12] demonstrated a negative association between CCF and survival in a study of 593 OHCA patients in Arizona employing a methodology similar to our study. While chest compression depth was found to be associated with improved survival (adjusted OR per 5 mm increase in compression depth 1.29 (95% CI 1.00–1.65), CCF (per 10% increase) was negatively associated with both survival OR 0.62 (0.39 to 1.00) and neurologically intact survival OR 0.48 (0.28 to 0.82).

Our findings regarding pre-shock pause deserve special consideration. Pre-shock pause duration <10 s remained a strong predictor of survival in our overall model OR 1.82 (1.29, 2.57) as well as our model of patients with no ROSC during the first 10 min of the resuscitation OR 1.82 (1.29, 2.57). This corroborates the findings of previous research[11,28–31] and suggests that pre-shock pause as an interruption in chest compressions (and hence impacting CCF during minutes in which a shock occurs) may not only predict survival but represent the most deleterious time to delay chest compressions. It is also possible that short pre-shock pause duration is critical to termination of VF with return of spontaneous circulation but that good quality CPR as measured by CCF may be required to maintain consistent cerebral blood flow particularly during prolonged resuscitations. The length and number of pauses (pre-shock and non- shock related pauses) that occur during resuscitation impact CCF but may do so in different ways. From our data base we are unable to determine whether a single long pause or multiple short pauses, which may both impact CCF similarly but may have different impacts on patient outcomes. Further research in this area may help clarify the role of pause length on CCF.

The impact of epinephrine on clinical outcomes during out-of-hospital cardiac arrest has drawn a great deal of scrutiny in recent resuscitation research.[32,33] Interestingly, we did note an increase in epinephrine administration for episodes with ROSC within 5–10 min (49.2%) and no ROSC within 10 min (87.0%) when compared to those with ROSC within 5 min (17.9%) consistent for worsening outcomes for patients with longer resuscitations, increasing epinephrine administration yet paradoxically higher CCF. The potential for epinephrine dosage confounding our results does exist.

Our study has several limitations. The primary exposure CCF was derived from the electronic defibrillator recording. Determination of CCF depended upon knowing when ROSC occurred in order to accurately ascertain the CCF denominator. Precise determination of the timing of ROSC can be challenging and may rely on estimates based on written reports, especially if audio was not available on the defibrillator recording. If inaccuracies occurred in determining the precise timing of ROSC, this circumstance would have a larger impact for bias in shorter resuscitations. Moreover, although the study included a median of 10 min of CPR process measurement, the CPR measurements still only captured on average about a third of the resuscitation. Whether the captured third is representative of the entire resuscitation is uncertain.

The study was observational and so we must consider confounding as an explanation for the observed relationships. We did not have complete information about other potential predictors such as compression depth which could be an unmeasured confounder. We as well did not control for the application of therapeutic hypothermia in our models. Similarly, we were unable to measure CPR quality by bystanders or by EMS providers prior to defibrillator pad application which may have underestimated CCF early in the resuscitation. For measured covariates, we attempted to control for confounding by using multivariable logistic regression. However the models may still provide residual confounding. For example, we created a variety of models to assess for the influence of resuscitation length on CCF, but there may still be some element of confounding by indication with longer resuscitation yielding higher CCF yet a lower number of survivors. Our data base lacked the granularity to assess for post-shock rhythm transitions and as such we were unable to assess whether cases in which defibrillation resulted in non-shockable rhythms (asystole or PEA) was associated with greater CCF, longer resuscitations and worse outcomes. Lastly, the study took place in regions with optimized EMS system response times and improved 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 this observational cohort study of OHCA patients presenting in a shockable rhythm, increasing CCF was paradoxically associated with lower odds of survival when adjusted for Utstein predictors, other CPR metrics and ROC site. The relationship between CCF and clinical outcomes was null in a sensitivity analysis restricted to patients without ROSC in the first 10 min. CCF is a complex measure and taken by itself may not be a consistent predictor of clinical outcome.

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Conflict of interest statement

Dr. Cheskes has received speaking honorarium and research funding on CPR quality from Zoll Medical and Physio Control. Dr. Cheskes has received grant funding as Co PI, Toronto site, Resuscitation Outcomes Consortium. Dr Stub is supported by a co-funded NHMRC/NHF early career fellowship (no. 1090302/100516).

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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.2015.07.003

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