Association Between Chest Compression Interruptions and Clinical Outcomes of Ventricular Fibrillation Out-of-Hospital Cardiac Arrest

Running title: Brouwer et al.; Association between long pauses in CPR and survival

Tom F. Brouwer, MD1; Robert G. Walker, BA2; Fred W. Chapman, PhD2; Rudolph W. Koster, MD, PhD1

1Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands; 2Physio Control, Inc., Redmond, WA

Address for Correspondence:
Tom F. Brouwer, MD
Academic Medical Center
Department of Cardiology, Room F3-241
PO Box 22700, Meibergdreef 9
1105 AZ Amsterdam, the Netherlands
Tel: 31-20-5661409
Fax: 31-20-5669618
E-mail: t.f.brouwer@amc.uva.nl

Journal Subject Code: Treatment:[25] CPR and emergency cardiac care
Abstract

Background—Minimizing pauses in chest compressions during cardiopulmonary resuscitation (CPR) is a focus of current Guidelines. Prior analyses found that prolonged pauses for defibrillation (peri-shock pauses) are associated with worse survival. We analyzed resuscitations to characterize the association between pauses for all reasons and both ventricular fibrillation termination and patient survival.

Methods and Results—In 319 patients with ventricular tachycardia/fibrillation out-of-hospital cardiac arrest, we analyzed recordings from all defibrillators used during resuscitation and measured durations of all CPR pauses. Median (25th, 75th percentile) durations in seconds were 32 (22, 52) for the longest pause for any reason, 23 (14, 34) for the longest peri-shock pause, and 24 (11, 38) for the longest non-shock pause. Multivariable regression models showed lower odds for survival per five second increase of the longest overall pause (OR 0.89, 95%CI 0.83-0.95), longest peri-shock pause (OR 0.85, 95%CI 0.77-0.93), and longest non-shock pause (OR 0.83, 95%CI 0.75-0.91). In 36% of cases, the longest pause was a non-shock pause; this subgroup had lower survival than cases where the longest pause was a peri-shock pause (27% vs 44% respectively, p<0.01) despite a higher chest compression fraction. Pre-shock pauses were 8 seconds (4, 17) for shock that terminated ventricular fibrillation and 7 seconds (4, 13) for shocks that did not (p=0.18).

Conclusions—Prolonged pauses have a negative association with survival not explained by chest compression fraction or decreased VF termination rate. VF termination was not the mechanism linking pause duration and survival. Strategies shortening the longest pauses may improve outcome.

Key words: heart arrest, cardiopulmonary resuscitation, defibrillation, survival
Introduction

Minimizing interruptions in chest compressions during cardiopulmonary resuscitation (CPR) is a prime focus of current Guidelines.\(^1\)\(^2\) Prolonged interruptions are considered to be particularly harmful, and have been observed to occur commonly during resuscitation from out-of-hospital cardiac arrest (OHCA).\(^3\)\(^-\)\(^7\) Prior clinical research evaluating the association between duration of individual interruptions and patient outcomes has focused on peri-shock pauses, interruptions associated with delivery of a defibrillation shock.\(^7\)\(^-\)\(^9\) However, chest compressions are commonly interrupted for reasons other than shock delivery.\(^10\) The significance of long interruptions for reasons other than shock delivery, non-shock pauses, has not been clinically evaluated.

In two cohorts of out-of-hospital cardiac arrest patients with initial ventricular fibrillation (VF) or ventricular tachycardia (VT), Cheskes et al. found a negative association between the duration of the longest peri-shock interruption over the first up-to-three shocks and survival to hospital discharge.\(^7\)\(^\)\(^8\) The investigators postulated that the detrimental effect of prolonged peri-shock interruptions might be due to a correlation between peri-shock interruptions and chest compression fraction, a CPR quality metric which has separately been reported to have a significant association with patient outcome.\(^11\)\(^-\)\(^13\) In a small cohort of in-hospital and out-of-hospital arrest patients, Edelson et al. found a negative association between pre-shock pause length and successful VF termination.\(^14\) This observation has also been posited as a mechanistic explanation for the association between long peri-shock pauses and poor survival.\(^7\)

We analyzed a cohort of out-of-hospital resuscitations to characterize the association between interruptions in chest compressions for all reasons and patient survival. We also evaluated whether the duration of the pre-shock chest compression interruption was associated with the ability of a shock to terminate the arrhythmia for which it was delivered.
Methods

Setting

We conducted an observational study of prospectively collected data from the Amsterdam Resuscitation Study (ARREST), an ongoing registry of all out-of-hospital cardiac arrests (OHCA) in the Dutch province of North Holland, which has a population of approximately 2.4 million inhabitants. Basic life support (BLS) throughout this study was performed with a compression:ventilation ratio of 30:2. Advanced Life Support (ALS) was performed according to ERC Guidelines, including administration of epinephrine and amiodarone, and airway protection by endotracheal intubation. Details of the ARREST registry have been described previously. Briefly, data from all OHCA were collected according to the Utstein recommendations, including demographic and response data obtained from dispatch records and prehospital provider documentation, information verbally reported by EMS personnel, data from ambulance defibrillators and all automated external defibrillators (AED) used, and hospital survival data including neurological outcomes at discharge obtained from hospital medical records. Timing of ALS interventions and dose of drug administered was not recorded in the ARREST database.

The Medical Ethics Review Board of the Academic Medical Center in Amsterdam approved the study and gave a waiver for the requirement of informed consent as only routinely collected data were analyzed.

Data collection

We included all cases of out-of-hospital cardiac arrest with a presumed cardiac cause occurring between January 1, 2009 and December 31, 2009 with an initial recorded rhythm of VF or VT, and for which continuous ECG and impedance recordings were available from all defibrillators used during the resuscitation attempt, including EMS and public access AEDs. Continuous
waveform data were analyzed by two independent reviewers to confirm the initial rhythm diagnosis and to measure CPR and resuscitation process metrics.

**Data analysis**

We identified each interruption in chest compressions longer than three seconds that occurred during the resuscitation attempt, and whether or not it was associated with delivery of a defibrillation shock. We chose a threshold of three seconds to be compatible with prior publications analyzing chest compression interruptions with the same monitors and data review software.7,8,11,12

We defined pre-shock interruptions as the interval from the last chest compression before the shock to the instant of shock delivery, and post-shock interruptions as the interval from the instant of shock delivery to the first post-shock chest compression. Peri-shock interruptions were defined as the sum of pre-and postshock pauses around one shock. For shocks delivered during uninterrupted chest compressions from a mechanical CPR device, we defined the duration of pre-shock, post-shock, and peri-shock interruptions each as 0 seconds. We excluded shocks for which pre-shock pauses or post-shock pauses could not be measured completely, for example when no chest compressions were performed between the beginning of the defibrillator recording and shock delivery. For any shock, if the result of the shock was immediate return of spontaneous circulation with no subsequent chest compressions, the post-shock interruption was defined as 0 seconds, and the end of the peri-shock interruption was defined as the instant of shock delivery.

We defined non-shock interruptions as intervals longer than 3 seconds without chest compressions and without delivery of a shock or without clear indication of return of spontaneous circulation. Clear indication of return of spontaneous circulation consisted of
absence of chest compressions with a narrow-complex organized rhythm > 40 beats per minute, and either a measured blood pressure or clear evidence of a cardiac output component in the impedance signal, synchronous with each ECG complex.\textsuperscript{16,17} For determination of the longest non-shock interruption, only interruptions between the beginning of the recording and delivery of the last shock were considered, in order to avoid potential confounding by interruptions associated with terminating efforts at the end of unsuccessful resuscitation attempts. This also ensured that the longest peri-shock and non-shock interruptions were measured over the same period of the resuscitation effort. Cases without any non-shock interruptions were excluded from analysis of the relationship between longest non-shock pause and survival, but were included in analyses of other categories of pauses.

Finally, we defined the longest overall interruption as the single longest interval without chest compressions and without a pulse prior to resumption of compressions after delivery of the last shock. For the longest overall interruption, longest peri-shock interruption, and longest non-shock interruption in each case, we measured the elapsed time from the beginning of the resuscitation attempt to the beginning of the respective interruption.

We measured chest compression fraction, defined as total time with chest compressions divided by the interval of measurement, for two different time periods; one from the beginning of the recording up to the last shock, and the other for the first five minutes of recorded data only. If there was an interval with clear indication of return of spontaneous circulation followed by rearrest, that interval was excluded from the measurement of chest compression fraction. For each shock, we determined VF termination outcome, defined as absence of VF for at least five seconds post-shock.\textsuperscript{14,18,19} For analysis of probability of VF termination, we excluded shocks where the pre-shock no-compression interval could not be measured in full.\textsuperscript{14} For each case, we
measured the interval to the last shock as the elapsed time from the beginning of the recorded ECG signal of the first defibrillator used during the attempt, until delivery of the last observed shock. We measured the duration of the resuscitation attempt as the elapsed time from the beginning of the recorded ECG signal of the first defibrillator used during the attempt, until the last observed chest compression or shock, whichever was later. Survival to discharge and Cerebral Performance Category (CPC) at discharge was determined from hospital records.

To address potential confounding from variability in the duration of resuscitation efforts prior to delivery of the last shock, we stratified all cases based on the interval to last shock, grouping cases into categories of 0-5 minutes, 5-10 minutes, 10-15 minutes, 15-20 minutes, and > 20 minutes. We then determined the median duration of the longest overall interruption, longest peri-shock interruption, and longest non-shock interruption for survivors and non-survivors within each stratum. Across the entire cohort, we also calculated the correlation between the duration of the longest overall chest compression interruption and the interval to last shock.

**Statistical analysis**

Continuous data were summarized as means (SD) or medians with percentiles (25th, 75th) when appropriate. Comparisons were performed using Student’s t-test for normally distributed data, the Mann-Whitney U test for non-normally distributed continuous data, and Chi-square for proportions. Trends were tested for significance with chi-square for trend. We used multivariable logistic regression to model the odds of survival and intact neurologic outcome (CPC 1-2 at discharge) as a function of the duration of the longest peri-shock, longest non-shock, and longest overall chest compression interruptions, adjusting for the Utstein predictors for survival and chest compression fraction. Chest compression fraction over the first five minutes of the
resuscitation was used in the model to minimize confounding from time-dependent optimization of the resuscitation process, such as transition to ALS strategies, which can increase overall chest compression fraction as the duration of resuscitation increases. We also performed a sensitivity analysis using chest compression fraction measured to the last shock. P-values <0.05 were considered statistically significant. All statistical analyses were performed in SPSS (IBM, version 21 for Windows, Chicago, IL).

Results

A total of 319 cases met our inclusion criteria and were analyzed (Figure 1). Survival to hospital discharge was 37.9% in this cohort, and did not differ significantly for the group of 98 excluded cases. Survivors and non-survivors differed significantly in age, location of the arrest, witness status, interval from call to first shock, chest compression fraction over the first five minutes, and duration of resuscitation attempt to the last shock (Table 1). A total of 113 of the 121 survivors (93%) were discharged with good neurologic outcome (CPC 1 or 2).

Interruptions in chest compressions and duration of resuscitation attempts

The median duration of the longest overall chest compression interruption through delivery of the last shock was 32 seconds (22, 52). The median duration of the longest peri-shock interruption was 23 seconds (14, 34). Median durations of the longest pre-shock and post-shock pauses were 16 (8, 22) and 8 seconds (5, 15), respectively. In 275 cases, at least one non-shock interruption occurred prior to the last shock. Median duration of the longest non-shock interruption was 24 seconds (11, 38); VF was the rhythm during 70% of these interruptions. Median chest compression fraction was 0.73 (0.61, 0.82) through the first five minutes of recorded data, and 0.79 (0.71, 0.84) through the last shock. The longest overall chest
compression interruption comprised a median 30% (19%, 57%) of the total time without chest compressions prior to delivery of the last shock. The contributions of the longest peri-shock and longest non-shock interruptions to the total time without chest compressions were a median 17% (11%, 38%) and 18% (11%, 27%), respectively.

The median elapsed time until delivery of the last shock, which marked the end of our analyzed interval in each case, was 10.5 (2.9, 18.9) minutes. This was a median 84% (45%, 100%) of the total elapsed time of the resuscitation attempt, with a median of 1.9 (0.0, 6.3) minutes of resuscitation efforts after delivery of the last shock. In 58 cases (18%), this portion of the resuscitation effort after delivery of the last shock contained a chest compression interruption longer than the longest interruption within our interval of analysis.

For each category of pause, the longest such pause occurred on average during the first several minutes of the resuscitation attempt. Median elapsed time at the beginning of the longest overall pause was 2.6 (0.3, 7.7) minutes. Results were similar between the longest peri-shock pause (3.8 (0.5, 8.3) minutes) and the longest non-shock pause (3.6 (1.7, 7.8) minutes). A total of 29 cases (9%) were treated with mechanical CPR at some point during the resuscitation attempt. In 7 cases (2%), the transition from manual to mechanical CPR was responsible for the longest overall interruption in chest compressions.

A total of 14 cases (4%) were treated with a public access AED prior to arrival of professional responders. In 8 of these cases, the longest overall pause occurred during use of the public access AED.

In 16 cases (5%), the patient arrested in the presence of EMS personnel: 4 in the presence of a police first responder, 4 in the presence of a BLS general practitioner, and 8 in the presence of ALS paramedics.
Survival and interruption duration

When grouped by duration of the longest peri-shock interruption, longest non-shock interruption, and longest overall interruption, cases with longer durations of each category of interruption exhibited significantly lower survival to hospital discharge (Figure 2). A similar trend with survival was observed for the longest pre-shock interruption, but not for the longest post-shock interruption (Table 2).

In 114 cases (36%), the longest overall interruption was a non-shock interruption. This subgroup had significantly lower survival than cases where the longest interruption was a peri-shock interruption (27% vs 44%, respectively, p<0.01), but it had a chest compression fraction that was slightly higher (0.74 versus 0.71, p=0.04).

In separate multivariable logistic regression models, adjusted for Utstein predictors for survival and for chest compression fraction, increasing durations of the longest overall pause, the longest peri-shock pause, and the longest non-shock pause were each associated with significantly lower odds of survival to discharge (Table 3). The significant associations for each type of longest pause remained unchanged when survival with good neurologic outcome (CPC 1 or 2) was substituted as the outcome variable (Supplemental Table 1). Results also did not differ when we used chest compression fraction measured up to the last shock, rather than over the first 5 minutes, in the regression model (data not shown).

When cases were stratified by duration of the resuscitation attempt in 5-minute groupings, the durations of the longest overall pause, longest peri-shock pause, and longest non-shock pause were consistently longer among non-survivors versus survivors for all three categories of pauses in all strata (Supplemental Table 2). Across all 319 cases, the duration of the longest overall pause was weakly correlated with the interval to the last shock (Spearman’s rho = 0.35).
**VF termination and interruption duration**

A total of 1105 shocks were delivered during a no-flow interval preceded by a recorded cessation of compressions. Post-shock compression artifact precluded conclusive determination of VF termination outcome for 34 of these shocks, and a further 23 shocks were inappropriately delivered to non-shockable rhythms. Thus, 1048 shocks were available for analysis of the relationship between the duration of the pre-shock interruption in chest compressions and probability of VF termination. The VF termination rate was 82% overall, 85% for the 902 biphasic shocks, and 64% for the 146 monophasic shocks. For first shocks only, these VF termination rates were 84%, 86%, and 73% respectively. Median duration of the pre-shock interruption was 8 seconds (4, 17) for shocks that successfully terminated VF, and 7 seconds (4, 13) for failed shocks (p=0.18). Results were similar when stratified by defibrillation waveform type: median pre-shock interruption duration was 8 seconds (4,17) for successful vs 7 seconds (5,15) for failed biphasic shocks (P=0.33), and 5 seconds (2,11) for successful vs 6 seconds (4, 9) for failed monophasic shocks (P=0.33).

When all shocks were grouped by duration of the pre-shock chest compression interruption in 10-second increments, there was a numerically small but statistically significant trend of increasing VF termination probability with increasing duration of the pre-shock interruption (p=0.01, Figure 3). Directionally similar, but not statistically significant trends were seen in subgroups of just first shocks (p=0.59), just biphasic shocks (p=0.06), just monophasic shocks (p=0.58), just AED shocks (p=0.29), and just manual shocks (p=0.12).

**Discussion**

Our study provides three important new findings linking CPR characteristics and survival. First,
the duration of the single longest interruption in chest compressions, irrespective of the reason for this pause, has a strong negative association with survival. Second, prolonged interruptions for reasons other than shock delivery have an equally strong association with survival as found earlier for prolonged peri-shock interruptions. Third, our data indicate that there is no association between the duration of the pre-shock pause and termination of ventricular fibrillation, and therefore the observed association with survival is not a consequence of any impact of pre-shock pause duration on defibrillation probability.

Our study differs from previous studies in that it evaluated the impact of interruptions in chest compressions offering a more complete analysis of the cardiac arrest. We obtained records from all defibrillators used during resuscitation, including public access AEDs. This helped in two ways; it allowed us to identify cases initially in VF directly from the electrocardiogram rather than inferring this from information that an AED had delivered a shock, and it enabled us to measure interruptions over almost the entire resuscitation effort, excluding only bystander CPR prior to defibrillator attachment. As a result, we could measure and control for chest compression fraction in our analysis of the effect of pauses. We measured peri-shock pauses for every shock delivered to each patient, including effects of interruptions for shocks delivered beyond the first few minutes of resuscitation efforts. Most importantly, we evaluated all chest compression interruptions regardless of the reason instead of just peri-shock pauses. This enabled us to consider the question of whether interruptions for defibrillation are more detrimental than interruptions for other reasons.

There are many reasons that chest compressions are interrupted during resuscitation attempts, and our results suggest that any prolonged pause is harmful. We found a strong negative association between duration of the longest pause (for any reason) and survival to
hospital discharge; in a multivariable model, the odds ratio for survival was 0.89 for each additional five seconds in duration of the longest pause (Table 3), after adjusting for chest compression fraction and the Utstein predictors. The strength of the association between the longest non-shock pause and survival was similar to the strength of the association between the longest peri-shock pause and survival. Therefore, shortening pauses for reasons other than shock delivery may warrant as much attention as has recently been given to shortening pauses for shock delivery.

A single prolonged pause can substantially reduce the chest compression fraction for a case, and some of the previous work has found a significant association between chest compression fraction and survival. In our data, the longest overall pause was responsible for one-third of the cumulative time without chest compressions. Nevertheless, a significant association remained between the duration of the longest pause and survival even after we adjusted for chest compression fraction. Prior studies indicate that the relationship between chest compression fraction and survival to hospital discharge is complex.11-13 Our observations suggest that individual long pauses are more harmful than multiple short pauses, even if overall chest compression fraction is similar. Experimental studies have shown that, when compressions are paused, blood flow begins to taper off right away but does not completely halt for at least a few seconds.20 Perhaps this residual flow early in a pause keeps that part of the pause from being as harmful. Thus while chest compression fraction may have conceptual value in summarizing the goal of minimizing interruptions in chest compressions, it may be significantly confounded as a predictive clinical metric, and less useful than a metric that additionally considers the duration of individual interruptions.

Rescuers typically interrupt compressions to defibrillate, and it is widely understood that
these peri-shock pauses should be kept brief. Two prior analyses have found a negative association between survival and the duration of the longest peri-shock pause, but restricted their analysis to the first three shocks.7,8 Our study confirms and extends that understanding; we looked across all shocks and found that duration of the longest peri-shock pause (and longest pre-shock pause) were each associated with worse survival (Table 2). We also performed an analysis restricted to the first three shocks, and found similar results (data not shown).

Prolonged resuscitation attempts, which are more common in non-survivors than among survivors, allow more time for prolonged interruptions in chest compressions to occur. It is therefore possible that a prolonged interruption is simply a marker of a more prolonged resuscitation attempt, and that the duration of the resuscitation attempt is the more significant factor influencing outcomes. To analyze this potential confounding effect of resuscitation duration, we stratified cases into groups based on the interval to the last shock. The duration of the longest overall pause, longest peri-shock pause, and longest non-shock pause was longer for non-survivors vs survivors in every stratum. Additionally, the longest overall interruption typically occurred during the first few minutes of the resuscitation attempt, and its duration was only weakly correlated to resuscitation duration across our entire cohort. This suggests that prolonged interruptions are not simply a surrogate for resuscitation duration.

Our results show clearly that longer pre-shock pauses were not associated with lower VF termination rate; we observed that the rate was constant over the range of pre-shock pause durations. This finding is consistent with other reports. In 845 OHCA patients randomized to two protocols, Jost et al. reported a substantial difference in pre-shock pause duration (9 vs. 19 s) but no difference in VF termination between groups.21 In 223 OHCA patients, Kramer-Johansen et al. compared defibrillation using manual vs AED mode, and found a significant difference in pre-
shock pause duration (15 vs. 22 s) but no difference in VF termination rate (61% vs 60%),
despite a higher rate of post-shock pulse generating rhythms in the manual defibrillation arm (7% vs 3%).
In an analysis of 912 patients enrolled in the CIRC trial, Olsen et al. found no association between pre-shock pause duration and VF termination rate during manual CPR, and a significant positive association during mechanical CPR, with VF termination rate increasing as pre-shock pause duration increased.

What might connect pre-shock pause length and survival? A previously hypothesized mechanism is that longer pauses lead to decreased probability of VF termination which leads to worse survival. This mechanism cannot explain our results, because the significant decrease in survival we observed when the pre-shock pause was prolonged was not accompanied by any decrease in VF termination rate for long pre-shock pauses. Another hypothesized mechanism is that the metabolic status of the myocardium might deteriorate rapidly during pauses, and the post-shock mechanical and electrical function of the heart might be extremely sensitive to the metabolic status of the myocardium at the moment of shock administration. A commonly accepted implication of this hypothesis is that peri-shock pauses are more harmful than pauses elsewhere during the resuscitation. Our data show that prolonged non-shock pauses have as strong a negative association with survival as prolonged peri-shock pauses. It is possible that distinct mechanisms are responsible for the apparent detrimental effect of long peri-shock pauses compared to long non-shock pauses. Alternately, it is possible that the global ischemia from any prolonged interruption in CPR-generated blood flow is harmful, independent of the specific metabolic status of the heart at the time of shock delivery.

**Clinical implications**

Our findings may have implications for resuscitation strategy and clinical care. Our data imply
that the focus now placed on minimizing peri-shock pauses should be broadened, and that similar emphasis should be placed on eliminating or minimizing pauses for other interventions as well. Examples of these include pauses for intubation, handoff of care from first responder to paramedics, pulse check, and moving the patient. Based on our findings, reducing pauses for those interventions may be more important than further reducing pauses for defibrillation. Another implication is that, if a resuscitation team needs to perform multiple interventions requiring interruption of compressions, it might be better to perform them individually with compressions interspersed than to cluster them together into one longer pause. Such stacking of multiple interventions into a single prolonged pause has been identified in at least one report as a likely explanation for the observed prevalence of excessively long interruptions.

Limitations
This study can only assess the association between pauses and survival, and cannot establish a causal relationship. It could be that the variable we chose to measure and associate with survival is only a marker for the true causal factor(s). Our data did not allow identification of the specific reason for prolonged non-shock or peri-shock chest compression pauses. We cannot rule out the possibility that some other unmeasured aspect of CPR quality, resuscitation technique, resuscitation circumstance, or patient condition is associated with long CPR interruptions and that this factor, rather than the prolonged pause itself, reduces the chance of survival.

Conclusions
We found that duration of the single longest pause in chest compressions has a significant negative association with survival to hospital discharge in patients suffering OHCA presenting with VF or VT. The duration of non-shock pauses has as strong a negative association with
survival as the duration of peri-shock pauses. Pre-shock pause duration is also associated with survival, but since it was not meaningfully associated with VF termination, modulation of defibrillation efficacy cannot be the mechanistic link between pause duration and survival. Minimizing interruptions in chest compressions is important for improving outcomes from OHCA and attention should be focused on shortening the longest interruptions, regardless of their cause.

Acknowledgments: We thank Stefanie Beesems for her support and Loes Bekkers, Paulien Homma and Remy Stieglis for data management.

Funding Sources: The ARREST data collection is maintained by an unconditional grant of Physio Control Inc, Redmond, WA, USA.

Conflict of Interest Disclosures: Authors Chapman and Walker are employees of Physio-Control, which manufactures and markets defibrillators and other resuscitation products. Dr. Brouwer received support for living expenses during an internship with Physio-Control.

References:


4. Wang HE, Simeone SJ, Weaver MD, Callaway CW. Interruptions in cardiopulmonary


**Table 1.** Baseline characteristics of the analyzed cohort.

<table>
<thead>
<tr>
<th></th>
<th>All (n = 319)</th>
<th>Survivors (n = 121)</th>
<th>Non-survivors (n = 198)</th>
<th>P value (Survivors vs Non-survivors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td>64.3 ± 15.2</td>
<td>57.0 ± 14.8</td>
<td>68.7 ± 13.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>81%</td>
<td>79%</td>
<td>82%</td>
<td>0.59</td>
</tr>
<tr>
<td>Public Location</td>
<td>41%</td>
<td>54%</td>
<td>34%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Witnessed arrest</td>
<td>84%</td>
<td>93%</td>
<td>79%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Call to first shock interval (minutes; median, 25th, 75th percentile)</td>
<td>10.2</td>
<td>8.9</td>
<td>10.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>80%</td>
<td>82%</td>
<td>80%</td>
<td>0.58</td>
</tr>
<tr>
<td>Chest compression fraction over first 5 minutes (median, 25th, 75th percentile)</td>
<td>0.73</td>
<td>0.71</td>
<td>0.74</td>
<td>0.04</td>
</tr>
<tr>
<td>Duration of resuscitation to last shock (minutes; median, 25th, 75th percentile)</td>
<td>10.5</td>
<td>4.0</td>
<td>14.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Number of shocks</td>
<td>4 (2, 7)</td>
<td>2 (1, 5)</td>
<td>4 (3, 7)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Table 2.** Survival to hospital discharge as a function of the duration of the longest pause#.

<table>
<thead>
<tr>
<th>Pause duration</th>
<th>&lt;10 sec</th>
<th>10-19 sec</th>
<th>≥20 sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Longest pre-shock pause (n=294)</td>
<td>43%</td>
<td>37%</td>
<td>24%</td>
</tr>
<tr>
<td>Longest post-shock pause (n=311)</td>
<td>37%</td>
<td>36%</td>
<td>35%</td>
</tr>
<tr>
<td>Longest peri-shock pause (n=288)</td>
<td>45%</td>
<td>24%</td>
<td>27%</td>
</tr>
<tr>
<td>Longest non-shock pause (n=278)</td>
<td>51%</td>
<td>24%</td>
<td>18%</td>
</tr>
<tr>
<td>Longest pause any cause (n=319)</td>
<td>56%</td>
<td>35%</td>
<td>32%</td>
</tr>
</tbody>
</table>

* Chi-square for trend

# for each category of pause, cases were only included if at least one of that type of pause could be fully measured
Table 3. Odds ratios (95% confidence intervals) of survival to discharge for four logistic regression models. (1) Unadjusted univariable regression model of survival based on each baseline variable. (2) Multivariable regression model of survival vs longest peri-shock pause, adjusted for all baseline variables. (3) Multivariable regression model of survival vs longest non-shock pause, adjusted for all baseline variables. (4) Multivariable regression model of survival vs longest overall pause, adjusted for all baseline variables.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Unadjusted Univariable model</th>
<th>Multivariable Longest peri-shock pause (n=288)</th>
<th>Multivariable: Longest non-shock pause (n=275)</th>
<th>Multivariable: Longest Overall pause (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 1-year increase)</td>
<td>0.95 (0.93-0.96)</td>
<td>0.94 (0.92-0.96)</td>
<td>0.94 (0.92-0.96)</td>
<td>0.94 (0.92-0.96)</td>
</tr>
<tr>
<td>Male</td>
<td>0.85 (0.48-1.51)</td>
<td>0.54 (0.27-1.08)</td>
<td>0.56 (0.27-1.16)</td>
<td>0.62 (0.31-1.22)</td>
</tr>
<tr>
<td>Public location</td>
<td>2.27 (1.43-3.61)</td>
<td>1.51 (0.84-2.74)</td>
<td>1.41 (0.76-2.62)</td>
<td>1.62 (0.92-2.84)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>3.25 (1.52-6.96)</td>
<td>2.87 (1.20-6.87)</td>
<td>2.12 (0.86-5.19)</td>
<td>2.66 (1.13-6.26)</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>1.18 (0.66-2.01)</td>
<td>0.96 (0.45-2.05)</td>
<td>0.73 (0.33-1.61)</td>
<td>1.81 (0.40-1.66)</td>
</tr>
<tr>
<td>Call to first shock interval (per 1 minute)</td>
<td>0.88 (0.83-0.93)</td>
<td>0.88 (0.81-0.94)</td>
<td>0.89 (0.83-0.96)</td>
<td>0.88 (0.82-0.94)</td>
</tr>
<tr>
<td>Chest compression fraction over first 5 minutes (per 10% increase)</td>
<td>0.81 (0.71-0.92)</td>
<td>0.97 (0.79-1.21)</td>
<td>0.89 (0.72-1.11)</td>
<td>0.80 (0.67-0.96)</td>
</tr>
<tr>
<td>Longest peri-shock pause (per 5 second increase)</td>
<td>0.85 (0.84-0.98)</td>
<td>0.77 (0.77-0.93)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Longest non-shock pause (per 5 second increase)</td>
<td>0.83 (0.77-0.91)</td>
<td>N/A</td>
<td>0.83 (0.75-0.91)</td>
<td>N/A</td>
</tr>
<tr>
<td>Longest overall pause (per 5 second increase)</td>
<td>0.92 (0.88-0.97)</td>
<td>N/A</td>
<td>N/A</td>
<td>0.89 (0.83-0.95)</td>
</tr>
</tbody>
</table>
Figure Legends:

**Figure 1.** Flowchart of study cohort and exclusions. The final analysis included 76% of patients presenting with initial VT/VF. The last step of the flowchart presents the number of patients and type of pause that could be measured according to the definition as described in the methods section.

**Figure 2.** Survival to hospital discharge and duration of longest overall pause (black), longest peri-shock pause (light grey) and longest non-shock pause (dark grey). Numbers in bars represent the number of patients. Chi-square for trend: \( p<0.01 \) for each pause category, see also Table 2.

**Figure 3.** VF termination efficacy for first shocks (black) and all shocks (grey) grouped by pre-shock pause duration. Numbers in bars represent the number of shocks. For 240 out of 319 first shocks the pre-shock pause could be measured between cessation of chest compressions and shock delivery. Chi-square for trend: \( p=0.59 \) for first shocks, \( p=0.01 \) for all shocks (trend towards increasing VF termination probability with increasing duration of the pre-shock pause).
Figure 1

1168 EMS Treated OHCA

\[ \downarrow \]

751 Initial Rhythm Not VT/VF

417 Initial Rhythm VT/VF

\[ \downarrow \]

9 Non Cardiac Cause

408 Presumed Cardiac Cause

\[ \downarrow \]

82 Complete ECG not available from all defibrillators used during event

326 Complete ECG Recording

\[ \downarrow \]

7 No shocks or ICD Shocks

319 Included in Analysis

\[ \downarrow \]

294 Pre-shock pauses

\[ \downarrow \]

311 post-shock pauses

\[ \downarrow \]

288 peri-shock pauses

\[ \downarrow \]

275 non-shock pauses

\[ \downarrow \]

319 longest pauses
Figure 2

Survival rate vs. Duration pause length (seconds)

- Longest overall pause
- Longest peri-shock pause
- Longest non-shock pause

Numbers: 59 121 111 for <20 seconds, 130 115 96 for 20-39 seconds, 130 52 68 for >39 seconds.
Figure 3
Association Between Chest Compression Interruptions and Clinical Outcomes of Ventricular Fibrillation Out-of-Hospital Cardiac Arrest

Tom F. Brouwer, Robert G. Walker, Fred W. Chapman and Rudolph W. Koster

_Circulation._ published online August 7, 2015;

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circ.ahajournals.org/content/early/2015/08/07/CIRCULATIONAHA.115.014016

Data Supplement (unedited) at:

http://circ.ahajournals.org/content/suppl/2015/08/07/CIRCULATIONAHA.115.014016.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/
**Supplemental Table 1:** Odds ratios (95% confidence intervals) of survival with good neurologic outcome (CPC 1 or 2) for four logistic regression models. (1) Unadjusted univariable regression model of survival based on each baseline variable. (2) Multivariable regression model of survival vs longest peri-shock pause, adjusted for all baseline variables. (3) Multivariable regression model of survival vs longest non-shock pause, adjusted for all baseline variables. (4) Multivariable regression model of survival vs longest overall pause, adjusted for all baseline variables.

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Unadjusted Univariable model</th>
<th>Multivariable: Longest peri-shock pause (n=288)</th>
<th>Multivariable: Longest non-shock pause (n=275)</th>
<th>Multivariable: Longest overall pause (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 1-year increase)</td>
<td>0.95 (0.93-0.97)</td>
<td>0.95 (0.95-0.97)</td>
<td>0.95 (0.93-0.97)</td>
<td>0.95 (0.93-0.97)</td>
</tr>
<tr>
<td>Male</td>
<td>0.89 (0.50-1.58)</td>
<td>0.57 (0.28-1.17)</td>
<td>0.61 (0.29-1.23)</td>
<td>0.65 (0.32-1.28)</td>
</tr>
<tr>
<td>Public location</td>
<td>2.36 (1.48-3.77)</td>
<td>1.65 (0.91-3.00)</td>
<td>1.56 (0.84-2.89)</td>
<td>1.71 (0.97-3.00)</td>
</tr>
<tr>
<td>Bystander witnessed</td>
<td>2.87 (1.34-6.15)</td>
<td>2.87 (1.20-6.87)</td>
<td>1.80 (0.73-4.39)</td>
<td>2.22 (0.95-5.23)</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>1.12 (0.63-2.01)</td>
<td>0.93 (0.43-2.01)</td>
<td>0.70 (0.32-1.55)</td>
<td>0.78 (0.38-1.60)</td>
</tr>
<tr>
<td>Call to first shock interval (per 1 minute)</td>
<td>0.88 (0.83-0.93)</td>
<td>0.87 (0.81-0.94)</td>
<td>0.89 (0.82-0.96)</td>
<td>0.88 (0.82-0.94)</td>
</tr>
<tr>
<td>Chest compression fraction over first 5 minutes (per 10% increase)</td>
<td>0.79 (0.70-0.91)</td>
<td>0.93 (0.75-1.15)</td>
<td>0.86 (0.69-1.08)</td>
<td>0.78 (0.65-0.94)</td>
</tr>
<tr>
<td>Longest peri-shock pause (per 5 second increase)</td>
<td>0.90 (0.83-0.98)</td>
<td>0.84 (0.76-0.93)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Longest non-shock pause (per 5 second increase)</td>
<td>0.84 (0.78-0.92)</td>
<td>N/A</td>
<td>0.84 (0.76-0.92)</td>
<td>N/A</td>
</tr>
<tr>
<td>Longest overall pause (per 5 second increase)</td>
<td>0.92 (0.87-0.97)</td>
<td>N/A</td>
<td>N/A</td>
<td>0.89 (0.83-0.95)</td>
</tr>
</tbody>
</table>
**Supplemental Table 2:** Median duration of the longest overall pause, longest peri-shock pause, and longest non-shock pause stratified by interval to the last shock.

<table>
<thead>
<tr>
<th>Interval to the last shock</th>
<th>Longest overall pause</th>
<th>Longest peri-shock pause</th>
<th>Longest non-shock pause</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Non-survivors</strong> N=7</td>
<td>20 (14,25) sec</td>
<td>24 (17,27) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Survivors</strong> N=49</td>
<td>14 (10,22) sec</td>
<td>13 (9,22) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Interval to the last shock = 5-10 minutes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Non-survivors</strong> N=17</td>
<td>27 (17,43) sec</td>
<td>20 (14,27) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Survivors</strong> N=24</td>
<td>26 (11.42) sec</td>
<td>16 (11,32) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Interval to the last shock = 10-15 minutes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Non-survivors</strong> N=34</td>
<td>29 (23,43) sec</td>
<td>25 (16,34)sec</td>
</tr>
<tr>
<td></td>
<td><strong>Survivors</strong> N=26</td>
<td>24 (16,33)sec</td>
<td>19 (15,27) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Interval to the last shock = 15-20 minutes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Non-survivors</strong> N=36</td>
<td>33 (24,57) sec</td>
<td>24 (13,31 )sec</td>
</tr>
<tr>
<td></td>
<td><strong>Survivors</strong> N=8</td>
<td>26 (20,34) sec</td>
<td>20 (18,25) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Interval to the last shock &gt; 20 minutes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Non-survivors</strong> N=104</td>
<td>39 (28,59) sec</td>
<td>28 (17,38) sec</td>
</tr>
<tr>
<td></td>
<td><strong>Survivors</strong> N=14</td>
<td>32 (24,58) sec</td>
<td>26 (19,46) sec</td>
</tr>
</tbody>
</table>