Resumption of Chest Compressions Following Successful Defibrillation and Risk for Recurrence of Ventricular Fibrillation in Out-Of-Hospital Cardiac Arrest

Running title: Conover et al.; Chest compressions and VF recurrence in OHCA

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Abstract:

**Background** - Prior investigation of out-of-hospital cardiac arrest (OHCA) has raised the concern that ventricular fibrillation (VF) recurrence may be triggered by chest compression (CC) resumption. We investigated predictors of VF recurrence after defibrillation, including timing of CC resumption.

**Methods and Results** - Patients with witnessed OHCA and initial rhythm of VF from an Utstein-style database were analyzed. For each shock that defibrillated VF, CC resumption and VF recurrence times were determined. Shocks were classified according to post-shock rhythm. Factors (age, gender, time from dispatch to monitor/defibrillator application, and CC resumption) that could predict VF recurrence were analyzed. CC resumption was categorized into groups: CC1: 1-5 sec, CC2:6-10 sec, CC3: 11-30 sec, and CC4: >30 sec. 88 subjects were analyzed, with a total of 285 shocks, with 226 shocks that achieved asystole (N=102), organized rhythm (OR) (N=120) or monomorphic ventricular tachycardia (N=4). Following a successful shock, CC resumption occurred at a median [interquartile range] = 8 [5, 18] sec. VF recurred after 166 shocks (74%), and recurred within 30 sec in 69 shocks. There was no significant relationship between VF recurrence and factors analyzed including CC resumption time, nor stratified by post-shock rhythm. The hazard ratios for VF recurrence within 30 sec for later CC groups (CC2, CC3 and CC4) relative to early CC resumption (CC1) were: HR(CC2)=1.05 (p=0.9), HR(CC3)=1.75 (p=0.1), HR(CC4)=0.67 (p=0.4).

**Conclusions** - VF recurrence within 30 sec of a defibrillatory shock was not dependent upon timing of CC resumption in patients with witnessed arrest and initial rhythm of VF.

**Key words:** cardiopulmonary resuscitation, heart arrest, ventricular fibrillation, chest compression resuscitation
Introduction

Over the past ten years, the CPR guidelines for the treatment of ventricular fibrillation (VF) have been modified to increasingly emphasize the delivery of chest compressions (CC), by increasing the ratio of CC to ventilation, limiting the number of shocks to 1 rather than 3 stacked shocks, and increasing the duration of CC between shocks from 1 to 2 minutes\(^1\)\(^-\)\(^3\). In parallel to these changes, the survival for VF arrest has improved. In 2010 the survival to hospital discharge for cardiac arrest with witnessed VF in the Resuscitation Outcomes Consortium database was 28.4\(^\%\)\(^4\), increased from prior estimates of 17.7\(^\%\)\(^5\). Chest compressions are further emphasized in chest compression only CPR for bystanders and cardiocerebral resuscitation for emergency medical personnel, which has resulted in a further improvement in survival for witnessed cardiac arrest due to ventricular fibrillation, rising up to 33.7\(^\%\) in Arizona\(^6\).

Despite these improvements in survival over the past several years, there has remained the concern that CC may trigger the recurrence of VF. VF recurrence is common during resuscitation\(^7\)\(^-\)\(^11\) and the triggers are unclear. In an analysis of cardiac arrest victims in the Netherlands\(^12\) it was found that VF was highly likely to recur within the first 2 seconds after the re-initiation of CC, regardless of whether CC were resumed immediately after the shock or delayed for a post-shock rhythm analysis. Another investigation of cardiac arrest victims in Rochester, MN\(^13\) suggested that the risk of VF recurrence during CC was related to the post shock rhythm, finding that VF was more likely to recur during CC delivered to post-shock asystole.

We have investigated predictors for VF recurrence after defibrillation, including timing of CC resumption in a cohort of witnessed cardiac arrest victims in Arizona with initial rhythm of VF. Our hypothesis was that the risk of VF recurrence in the first 30 seconds post shock is
unrelated to when CC are resumed.

Methods

Resuscitation data from adult patients with witnessed OHCA was collected through the Saving Hearts in Arizona Registry and Education (SHARE) Program, a previously described statewide Utstein-style database. Out-of-hospital cardiac arrest has been designated a major public health problem by the Arizona Department of Health Services. SHARE is the designated public health program created to measure response to out-of-hospital cardiac arrest and improve outcomes. Thus, the SHARE Program initiatives and its data collection are exempt from the Health Insurance Portability and Accountability Act. By virtue of SHARE being a health department-sponsored public health initiative, the Arizona Department of Health Services’ Human Subjects Review Board and the University of Arizona institutional review board have determined that neither the interventions nor their evaluation constitutes human subjects research and have approved the publication of deidentified data.

Data for this investigation was taken from two sites in Arizona participating in the SHARE Program, from 2008 through 2011. The details of the methodology for data collection in the SHARE database have been described previously. Inclusion criteria were OHCA with resuscitation initiated in the field. Exclusion criteria included age less than 18 years, unwitnessed arrest, or initial rhythm other than ventricular fibrillation. Return of spontaneous circulation was defined as a confirmed pulse for at least 5 minutes.

Cardiac waveforms were downloaded from the defibrillator (ZOLL Medical Corporation) and inspected using RescueNet Code Review (ZOLL Medical Corporation). Analysis of shock outcome was made at 5 seconds after the shock. Shocks that successfully defibrillated VF were further classified as an organized rhythm (OR) if at least two QRS complexes were present and
otherwise as asystole. A shock outcome of ventricular tachycardia (VT) was made if a wide complex monomorphic tachycardia was present at 5 seconds post shock. Defibrillation of VF was considered successful if VF was terminated for at least five seconds after shock delivery, while the presence of polymorphic ventricular tachycardia (or VF) was regarded as a failure of defibrillation. Resumption of chest compressions (CC) was identified by CPR artifact and the presence of at least 3 seconds of uninterrupted CPR bars, derived by the defibrillator from the accelerometer signal (Figure 1). Time to chest compression resumption post shock was further categorized to four pre-specified CC groups: 1-5 seconds (CC1), 6-10 seconds (CC2), 11-30 seconds (CC3) and greater than 30 seconds (CC4). Shock outcome and time to recurrence of chest compressions were determined by two observers (ZC and JI). The ECG waveform was filtered for CPR artifact by the manufacturer’s software (ZOLL Medical Corporation) to allow visualization of the underlying rhythm, and time to recurrence of VF was determined by one observer (JI). Excluded were cases with significant artifact that obscured the underlying rhythm including loss of pad contact following the shock. Figure 1 shows an example of an ECG recording that includes filtering and the determination of CC resumption and VF recurrence.

**Statistical Analysis**

Continuous variables are presented as the median with interquartile range [25th, 75th percentile]. Statistical tests were performed using STATA (StataCorp, College Station, TX). Simple linear regression analysis was utilized to analyze factors that could be associated with the time to VF recurrence after a successful defibrillatory shock for patients with VF recurrence, with a logarithmic transformation of the time to VF recurrence. Factors analyzed were age, gender, time from EMS dispatch to connection of the monitor/defibrillator and time to CC resumption after the shock. Additionally the analysis was stratified with respect to shock outcome of asystole or
organized rhythm. Generalized linear mixed models using random effects were used to account for correlations within an individual subject due to multiple shocks.

A Kaplan-Meier analysis with proportional hazards model was performed to examine the risk of VF recurrence in the first 30 seconds post shock, according to CC group; correlations within the same subject for multiple shocks were accounted for using the cluster option within STATA, and Efron’s method to handle ties. Subjects were also classified according to whether there was any shock followed by VF recurrence within 30 seconds; differences in proportions between any VF recurrence within 30 seconds and outcome (pre-hospital return of spontaneous circulation (ROSC), survival to hospital admission, or survival to hospital discharge) were assessed with a chi square analysis.

Results
A total of 88 adult witnessed OHCA cases with initial rhythm of VF from the SHARE database were analyzed, with a total of 285 shocks, median of 3 shocks per patient, range 1-11 (interquartile range: [1-4]) and 226 shocks that successfully defibrillated VF (Figure 2). One subject was excluded for an uncertain post shock rhythm (fine VF versus asystole in the presence of CC) and another subject where the pads were not in contact immediately post-shock. Pre-hospital ROSC was achieved in 41 subjects, survival to hospital admission in 52 subjects and survival to hospital discharge in 34 subjects. The first shock successfully defibrillated VF in 76 out of 88 subjects, whereas second and later shocks defibrillated VF 76% of the time. Re-arrest with VF after achieving ROSC was seen in 10 subjects, with VF recurring in a range from 1 to 17 minutes after ROSC was documented, with a median of 4 minutes and 45 seconds. Compression rate was 112 [101, 125] compressions/min with a compression depth of 2.0 [1.8, 2.3] inches. Out of 226 successful shocks, VF recurred following 166 (74%) shocks, after 39
[16, 120] sec post shock, and within 30 sec in 69 shocks. Patient and resuscitation characteristics are given in Table 1.

Following a successful shock, CC resumption occurred at 8 [5, 18] sec post shock. Numbers of successful shocks by CC group were: [CC1, CC2, CC3, CC4]=[59, 60, 56, 51], respectively (Table 2). Figure 3 compares the time of VF recurrence to CC resumption for shocks where VF subsequently recurs. Time of VF recurrence and CC resumption within the first 60 seconds post shock, distinguishing first and subsequent shocks is shown in Figure 3B.

Of the 226 shocks that defibrillated VF, 102 (45%) shocks resulted in asystole and 120 (53%) shocks to an organized rhythm other than monomorphic VT, and 4 (2%) shocks to monomorphic VT (Figure 2). VF recurred at 47 [24, 135] sec after 78 shocks that had resulted in asystole, and recurred at 32 [14, 76] sec after 84 shocks that had resulted in an organized rhythm other than monomorphic VT (Figure 3C). The time to CC resumption was 9 [6, 13] sec following shocks that resulted in asystole, and 8 [4, 21] sec following shocks that resulted in an organized rhythm other than monomorphic VT.

There was no statistically significant difference in the time to VF recurrence according to age, gender, or time from EMS dispatch to connection of the monitor/defibrillator, or CC resumption time, nor any significant relationship when stratified by shock outcome (asystole vs organized rhythm (OR)), (Table 3). There was no statistically significant difference between shock outcome types in the time to VF recurrence (P=0.32) or time to CC resumption (P=0.50).

A Kaplan-Meier analysis curve for VF recurrence within 30 seconds post shock is shown in Figure 4. There were no statistically significant differences in survival curves among the CC groups. Hazard ratios for VF recurrence within 30 sec for later CC groups (CC2, CC3 and CC4) relative to early CC resumption (CC1) were: HR(CC2)=1.05 (p=0.9), HR(CC3)=1.75 (p=0.1),
HR(CC4)=0.67 (p=0.4). Additionally, the proportion of subjects with any VF recurrence within 30 seconds was not significantly different among patients that did or did not survive to hospital admission (33% vs 50%, P=0.10) or discharge (38% vs 41%, P=0.82). However, the proportion of subjects with any VF recurrence within 30 seconds was lower among patients that did achieve pre-hospital ROSC, 29%, compared to patients that did not achieve pre-hospital ROSC, 51%, with a P=0.04.

Discussion

The principle finding of this study is that the recurrence of VF after a shock that succeeds in defibrillation is not related to the temporal sequence of resuming chest compressions. Of 226 shocks that defibrillated VF in a cohort of 88 patients with witnessed OHCA and initial VF, the hazard ratio for VF recurrence in the first 30 seconds was similar whether CC were resumed immediately or delayed after a shock. Additionally, there was no relationship between age, gender or time from EMS dispatch to connection of the monitor/defibrillator to the timing of VF recurrence.

It has been previously demonstrated that VF commonly recurs after a successful defibrillatory shock7-11. This investigation similarly finds that VF recurrence is a common event, occurring in our investigation following about three-quarters of successful defibrillatory shocks, and with early VF recurrence within 30 seconds in about one-third of shocks. We also found that the post-shock pause before resumption of CC after a successful defibrillatory shock was highly variable, with a median time of 8 sec (interquartile range of 5-18 sec). and exceeding 30 seconds in about one-quarter of successful shocks wherein VF recurred within 30 seconds (Table 2).

VF recurrence during resuscitation is likely due to multiple factors that are not well understood. Higher VF recurrence rates have been observed in the setting of myocardial
ischemia and during reperfusion, in a rabbit model\textsuperscript{17,18} and in swine models\textsuperscript{19,20}. Additionally it has been proposed that chest compressions can trigger VF recurrence by a commotio-cordis type mechanism\textsuperscript{21}, or by electrical depolarization from the chest compression itself resulting in a long-short electrical activation sequence, as observed in a swine model\textsuperscript{22}.

To explore the influence of the timing of CC resumption upon VF recurrence, we focused upon the first 30 seconds post shock, a time frame where the post-shock pause to CC resumption would be most variable\textsuperscript{23,24}. We found that the risk of early VF recurrence was not affected by when chest compressions were resumed. Figure 3 illustrates the lack of correlation between chest compression resumption and VF recurrence in this patient cohort, and there was no significant relationship by regression analysis. Furthermore, we found that VF recurred in the first 30 seconds in 11 out of 51 shocks (22\%) wherein chest compressions had not resumed until after 30 seconds post-shock.

A cohort of 136 patients randomized to receive either delayed or immediate post shock chest compressions (according to the CPR guidelines published in 2000 or 2005\textsuperscript{1,2} was analyzed by Berdowski et al\textsuperscript{12}. They examined the risk for VF recurrence after the first shock and found a high hazard ratio for VF to recur within the first 2 seconds of resuming chest compressions, regardless of CPR protocol (2000\textsuperscript{1} or 2005\textsuperscript{2} guidelines). Since the 2005 guidelines\textsuperscript{2} advocate an immediate resumption of chest compressions, this led to an earlier recurrence of VF in their study. Our investigation did not find a relationship between chest compression resumption and VF recurrence, but has important differences in methodology. Our analysis was restricted solely to witnessed arrest, whereas about 40\% of cases analyzed by Berdowski et al.\textsuperscript{12} were unwitnessed. We examined VF recurrences throughout the recorded resuscitation, employing a statistical correction for multiple shocks within the same subject, rather than the first shock.
alone. It is unknown whether the risk of VF recurrence in relationship to chest compressions may change over time within a specific subject, but there was no apparent difference in the scatter of VF recurrence and CC resumption (Figure 3B) between first and subsequent shocks in this investigation. It is also possible that chest compression quality may impact upon VF recurrence. While chest compression depth was not reported in the Berdowski et al\textsuperscript{12} investigation, we found that chest compressions delivered in the Arizona SHARE registry were of high quality, with a median compression depth of 2.0 inches (5.1 cm), exceeding what has been reported in the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest database\textsuperscript{23}.

We also analyzed VF recurrence and CC resumption according to post shock rhythm (Figure 3C). We found no statistically significant difference in the time to VF recurrence for shocks that resulted in asystole or shocks that resulted in an organized rhythm. There was similarly no statistically significant difference in the time to CC resumption for post-shock rhythms of asystole versus an organized rhythm. Additionally, we found no relationship by regression analysis between VF recurrence and CC resumption according to shock outcome. Our findings differ from what was reported in a previous investigation of VF recurrence in a cohort of 32 patients\textsuperscript{13}. In that study, VF recurred more commonly during CC when the post-shock rhythm was asystole, and otherwise was more likely to recur in the absence of CC when the post-shock rhythm was organized. A limitation of that investigation was that the duration of chest compressions prior to VF recurrence was not reported, nor was the timing of either CC resumption or VF recurrence relative to the shock.

It is well known that in addition to maintaining a high fraction of time with chest compressions, there should also be an adequate depth, rate and chest wall recoil\textsuperscript{25, 26}, although the adoption of means to monitor CPR performance and implement quality improvement are
lacking. The 2010 American Heart Association Guidelines further dictate that CC be resumed immediately post shock without performing a rhythm check. However, there remains uncertainty as to how long the post-shock pause should be or can be without becoming detrimental. In a study of 815 patients in the Resuscitation Outcomes Consortium Epistry-Cardiac Arrest database, survival was lower if the preshock pause exceeded 20 seconds or the perishock (pre and post shock) pause exceeded 40 seconds. However, in that study survival was not affected by the duration of the post-shock pause. Thus the optimum post-shock delay to resuming chest compressions is unclear, but our investigation suggests that neither a brief nor prolonged post-shock pause affects the likelihood of VF recurrence.

Limitations
This is a retrospective analysis of cardiac arrest victims from two sites in Arizona, as part of the larger SHARE database, and future work will analyze data from other sites. Furthermore, timing of drug administration with respect to shocks and CC resumption was not analyzed. It is unknown whether drugs such as amiodarone or epinephrine may change the likelihood of VF recurrence in relationship to chest compressions. We observed a trend for a lower proportion of any VF recurrence within 30 seconds among patients that survived to hospital admission or discharge, however our sample size was not powered to detect a difference. The quality of the CPR filtered recordings was excellent, yet the visual identification of recurrence was determined by a single observer. In another similar study it was shown there was a 96% agreement between two observers in determining the onset of VF using a filtered signal. Therefore we feel it is unlikely that the lack of a second observer in this investigation to determine VF recurrence would have significantly affected our results.
Conclusions

In witnessed out of hospital cardiac arrest with an initial rhythm of ventricular fibrillation, VF recurred after successful defibrillation in about three-quarters of shocks. The risk of VF recurrence within 30 seconds after defibrillation was not affected by when chest compressions were resumed.

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Conflict of Interest Disclosures: Annemarie Silver is employed by ZOLL Medical. Bentley Bobrow and Daniel Spaite have an implementation grant that is from Medtronic Foundation to the University of Arizona and deemed by the Institutional Review Board as not human subjects research. Zacherie Conover, Julia Indik, and Karl Kern all have none.

References:


17. Wu TJ, Lin SF, Hsieh YC, Chen PS, Ting CT. Early recurrence of ventricular fibrillation...


### Table 1: Patient and Resuscitation Characteristics

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<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>88</td>
</tr>
<tr>
<td>*Age, years</td>
<td>64  [53, 71]</td>
</tr>
<tr>
<td>Women (%)</td>
<td>23</td>
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<tr>
<td>Cardiac Cause (%)</td>
<td>95</td>
</tr>
<tr>
<td>*Time from dispatch to monitor/defibrillator connection (min)</td>
<td>6.5 [5.5, 8.1]</td>
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<tr>
<td>Number of shocks</td>
<td>285</td>
</tr>
<tr>
<td>*Shocks/patient</td>
<td>3  [1, 4]</td>
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<tr>
<td>*Compressions/min</td>
<td>112 [101, 125]</td>
</tr>
<tr>
<td>*Compression depth (inches)</td>
<td>2.0 [1.8,2.3]</td>
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<tr>
<td>Subjects with pre-hospital ROSC‡</td>
<td>41</td>
</tr>
<tr>
<td>Subjects with survival to hospital admission</td>
<td>52</td>
</tr>
<tr>
<td>Subjects with survival to hospital discharge</td>
<td>34</td>
</tr>
<tr>
<td>Shock outcome:</td>
<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>Ventricular fibrillation</td>
<td>59</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>4</td>
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<tr>
<td>Asystole</td>
<td>102</td>
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<tr>
<td>Organized Rhythm (not ventricular tachycardia)</td>
<td>120</td>
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<tr>
<td>*CC† resumption, sec</td>
<td></td>
</tr>
<tr>
<td>All shocks</td>
<td>8  [5, 14]</td>
</tr>
<tr>
<td>For shocks that defibrillate VF</td>
<td>8  [5, 18]</td>
</tr>
<tr>
<td>*Ventricular fibrillation recurrence post shock, sec</td>
<td>39 [16, 120]</td>
</tr>
</tbody>
</table>

*Median [25th, 75th percentile]; †CC = chest compression; ‡ROSC = return of spontaneous circulation
Table 2: Early VF* recurrence (< 30 seconds post shock) by CC† group

<table>
<thead>
<tr>
<th></th>
<th>CC1(1-5sec)</th>
<th>CC2(6-10sec)</th>
<th>CC3(11-30sec)</th>
<th>CC4(&gt;30sec)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of successful defibrillatory shocks</td>
<td>59</td>
<td>60</td>
<td>56</td>
<td>51</td>
<td>226</td>
</tr>
<tr>
<td>VF* recurrence by 30 seconds (N, %)</td>
<td>17 (29%)</td>
<td>17 (28%)</td>
<td>25 (45%)</td>
<td>11 (22%)</td>
<td>70 (31%)</td>
</tr>
</tbody>
</table>

*VF = ventricular fibrillation; †CC = chest compression

Table 3: Predictors for Time to VF* Recurrence

<table>
<thead>
<tr>
<th></th>
<th>All Shocks with Subsequent VF Recurrence (N=166)</th>
<th>Shocks that Result in Asystole and with Subsequent VF Recurrence (N=78)</th>
<th>Shocks that Result in Organized Rhythm (Not Ventricular tachycardia) and with Subsequent VF Recurrence (N=84)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>P Value 0.200</td>
<td>P Value 0.099</td>
<td>P Value 0.934</td>
</tr>
<tr>
<td>Gender</td>
<td>P Value 0.089</td>
<td>P Value 0.052</td>
<td>P Value 0.374</td>
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<tr>
<td>Time from Dispatch to monitor/defibrillator connection</td>
<td>P Value 0.135</td>
<td>P Value 0.445</td>
<td>P Value 0.219</td>
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<tr>
<td>CC† Resumption</td>
<td>P Value 0.175</td>
<td>P Value 0.487</td>
<td>P Value 0.508</td>
</tr>
</tbody>
</table>

*VF = ventricular fibrillation; †CC = chest compression
Figure Legends:

**Figure 1:** Monitor/defibrillator recording including CPR bars for chest compressions (CC). The third shock results in an organized rhythm (first strip), and CC are resumed 12 seconds later as evidenced by CC artifact and immediately followed by the onset of CPR bars (second strip). The CPR filter is immediately applied, giving a filtered electrocardiogram (second strip), and VF recurrence is seen about 16 seconds after CC resumption (fourth strip). Recording exported using RescueNet Code Review (ZOLL Medical Corporation).

**Figure 2:** Subjects in the SHARE registry from two sites in Arizona with cardiac arrest due to an initial rhythm of VF. Patients were excluded if VF was unwitnessed, and two subjects were excluded due to waveform artifact or uncertain post shock rhythm, resulting in a total of 88 subjects analyzed (A). A total of 285 shocks were analyzed, of which 226 shocks successfully defibrillated VF to: asystole (102 shocks), organized rhythm (120 shocks) or monomorphic VT (4 shocks) (B)

**Figure 3:** Scatter plot of time to VF recurrence and time to resumption of chest compressions following shocks (A). The first 60 seconds following a shock is shown in (B) distinguishing first shocks from second and later shocks and in (C) distinguishing shocks that resulted in organized rhythm from those that resulted in asystole.

**Figure 4:** Kaplan-Meier analysis curve for VF recurrence within 30 seconds post shock, according to CC group. There was no significant difference in hazard ratios for VF recurrence
within 30 seconds for later onset of CC after 5 seconds (CC2, CC3, CC4) relative to early CC resumption (CC1). Hazard ratios for VF recurrence within 30 sec for later CC groups (CC2, CC3 and CC4) relative to early CC resumption (CC1) were: HR(CC2)=1.05 (p=0.9), HR(CC3)=1.75 (p=0.1), HR(CC4)=0.67 (p=0.4).
143 subjects with Initial Rhythm of VF

53 subjects with unwitnessed VF

90 subjects with witnessed VF

1 subject excluded for uncertain post-shock rhythm; 1 subject excluded due to loss of pad contact following shock

88 subjects analyzed
285 Total Shocks

59 Unsuccessful shocks (no defibrillation)

102 shocks resulting in asystole

120 shocks resulting in organized rhythm

4 shocks resulting in monomorphic ventricular tachycardia
The graph shows the relationship between CC resumption after shock (sec) and VF recurs after shock (sec). The data points are categorized into two groups: Organized Rhythm (X) and Asystole (●). The graph indicates a trend where as the CC resumption after shock increases, the VF recurs after shock decreases.
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