Delaying shock for cardiopulmonary resuscitation: does it save lives?
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\textbf{Purpose of review}  
Out-of-hospital cardiac arrest claims more than 450 000 lives annually in North America. Many communities have dedicated significant resources to provide rapid defibrillator response for patients in ventricular fibrillation. In spite of these efforts, mortality from out-of-hospital cardiac arrest has not improved significantly. Emerging evidence suggests some patients in ventricular fibrillation arrest may be harmed by immediate defibrillation.

\textbf{Recent findings}  
Recent laboratory studies have shown benefit in performing a period of chest compressions (cardiopulmonary resuscitation) prior to defibrillation in models with more than 4 minutes of induced ventricular fibrillation. During the initial 4 minutes the heart is more amenable to electrical defibrillation. Between 4–10 minutes, chest compressions create some coronary perfusion and fill the left ventricle to prepare the heart for electric shock. These findings, in conjunction with most emergency medical service response times reported to be 5–8 minutes, have prompted human investigation into a strategy of chest compression first. A recent randomized controlled trial reported a fivefold increase in survival for patients with more than 5 minutes of VF who received 3 minutes of chest compressions prior to defibrillation compared with those who had not.

\textbf{Summary}  
Current guidelines call for rapid defibrillation as the most important ‘link’ in the ‘chain of survival’. For most ventricular fibrillation patients who have professional rescuers arrive after 5–8 minutes of ventricular fibrillation, however, immediate defibrillation is likely to be ineffective. Counterintuitively, these patients may benefit from a period of chest compressions prior to being shocked.

\textbf{Keywords}  
defibrillation timing, out-of-hospital cardiac arrest, ventricular fibrillation

\textbf{Abbreviations}  

\begin{itemize}
  \item AED \textsuperscript{a} automated external defibrillator
  \item CPR \textsuperscript{b} cardiopulmonary resuscitation
  \item EMS \textsuperscript{c} emergency medical system
  \item OOH-CA \textsuperscript{d} out-of-hospital cardiac arrest
  \item PAD trial \textsuperscript{e} Public-Access Defibrillation and Survival After Out-of-Hospital Cardiac Arrest
  \item ROSC \textsuperscript{f} return of spontaneous circulation
  \item SCD \textsuperscript{g} sudden cardiac death
  \item VF \textsuperscript{h} ventricular fibrillation
\end{itemize}


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\section{Introduction}
Sudden cardiac death (SCD), defined as deaths occurring out of the hospital or in emergency departments due to cardiac disease, claims approximately 450 000 lives per year in the United States [1]. Despite reduction in overall mortality from cardiovascular disease, SCD rates remain elevated, especially in certain regions and populations of the United States [1]. Some resources have been dedicated to improving outcomes from SCD and out-of-hospital cardiac arrest (OOH-CA). Advanced life support units have increased their ability to quickly respond and apply more advanced care on scene. Basic life support units have been empowered to provide emergent cardiac care including cardiopulmonary resuscitation (CPR) and defibrillation using automated external defibrillators (AEDs). With increasing importance placed on rapid defibrillation and bystander CPR comes the implementation of telephone-assisted CPR and public access AEDs. In spite of these efforts, however, survival from OOH-CA is generally poor. Most areas report little improvement in SCD mortality, with survival still hovering around 3–5\% [1].

Studies of the effectiveness of improving the interventions have mixed results. In Seattle and Kings County, Washington, which by many is considered an OOH-CA success story, investigators reported an observed increase in survival to hospital discharge in the late 1970s–1980s from 7–17\% [2]. This came after efforts in CPR training for the public and increasing the number of emergency medical system (EMS) responder defibrillation-capable units. These results have been duplicated in few other communities (exception Rochester, MN) [3]. In New York City, survival is dismal, around 1.4\% [4]. Ontario, Canada, is only slightly better with 2.5\% survival [5]. When looking at studies of other locations, unfortunately the Seattle experience seems to be the outlier, not New York and Ontario. Further evaluation in Seattle showed that outcome improvements were not sustained [6]. Although it is true that epidemiologic studies in this area...
are difficult to compare because of statistical variations and definitions of SCD [7]. The efforts to improve results simply were not living up to the promise.

Why haven’t the millions of dollars in time and resources been effective in improving outcomes? Since the block grants of the 1970s, EMS response times were decreased and intervention capabilities were increased, in part for OOH-CA situations. Over the past decade several promising interventions have been studied, with modest overall impact. One that has shown promise, both in animals and preliminary human studies, has been to provide chest compressions prior to defibrillation for patients in a prolonged period of cardiac arrest. An increasing amount of clinical and laboratory evidence supports delaying defibrillation when cardiac arrest time is greater than 5 minutes. These early studies have shown significant mortality benefit for patients with prolonged ventricular fibrillation (VF) prior to defibrillation attempts. This paper addresses the question of whether it is better to delay shocking a person in VF until CPR can be performed.

Rapid defibrillation

Current clinical guidelines and clinical practice greatly emphasize the importance of rapid defibrillation for all patients with SCD in a shockable rhythm. The American Heart Association ‘chain of survival’ considers defibrillation to be the most important intervention and the ‘strongest link’ in the chain of survival for VF cardiac arrest intervention. The philosophy that ‘the earlier that the defibrillation is performed, the better the rate of survival’ is based on a small number of case series [1]. Based on these guidelines, rapid defibrillation is being taught to EMS providers as the most important intervention, possibly at the risk of suboptimal chest compressions. ‘Quick look’ defibrillator/monitor paddles allow the paramedic to determine whether a patient is in a ‘shockable’ rhythm and to provide that shock as a single intervention upon arrival at the patient’s side. In places where defibrillation can be nearly immediate, this approach has met with success. This was shown by a survival rate of 53% for people who collapsed with VF in a casino (74% for those who received the first shock within 3 minutes) [2] and 21% survival in a US airport when care was provide by teams of on-site personnel providing rapid defibrillation [3].

Delays in defibrillation

The main difference between the care from on-site rescuers (i.e., casino security guards or airport rescue crews) and the EMS agencies is the response time. The success of the casino and airport defibrillation strategies can be related to response times in the 2-minute to 3-minute range [5,6]. Even at their best, EMS response times are much longer. Ontario, Canada, reports an average response time of 7.8 minutes [4], Seattle, Washington 7.7 minutes [2], and Tucson, Arizona ~8 minutes [5]. Outside North America, these times were consistent in cities studied — Taipei 7.4 minutes [6] and Helsinki 7.0 minutes [7] — until arrival of EMS with defibrillator capability. Of note, the times reported in Seattle were after the improvements made in EMS aimed at decreasing response times. The time response difference of 2–3 minutes for the on-site providers vs the 7–8 minutes for EMS services, and the differences in outcomes, have prompted public and work force access to AEDs. This has also had mixed results, however. In Miami, publicly accessed AEDs improved time to first shock to 4.88 minutes from 7.64 [8], with improvement in survival from 9 to 17% for patients in VF. The recently published New England Journal of Medicine Public-Access Defibrillation and Survival After Out-of-Hospital Cardiac Arrest (PAD) trial, large multicenter study, showed a 9% absolute risk reduction and a twofold increased probability of survival for SCD patients who collapsed in a location with an AED available. An interesting finding from the study was the control group survival rate of almost 15% of definite cardiac arrests, although limitations in proportional interpretation are clear. The control group personnel were all trained and maintained in CPR [9]. For the study group with AEDs, the time until first rhythm assessment averaged more than 6 minutes. The PAD trial showed the benefit of AED placement and training lay persons in CPR, but also the difficulty and expense in placing AEDs and training people to use them to decrease the time to shock. The PAD study was unable to achieve response times of the casino or airport studies.

Importance of cardiopulmonary resuscitation

The studies looking at rapid (<3 minutes) on-site defibrillation (like the casino study) are limited in that they exclude the places where most arrests occur: residential facilities and private homes. The AED/CPR infrastructure of trained bystanders tested by PAD also excludes the vast majority of these residential dwellings. Several studies have shown the clinical benefit of CPR, either bystander or EMS provider. A multivariate analysis by Wilcox-Gok [10] showed a significantly higher probability of survival related to shorter elapsed time from collapse to initiation of CPR.

Animal studies have shown the importance of uninterrupted CPR of good quality. In a swine study by Kern [11], following 3 minutes of untreated VF, pigs were grouped to receive either standard 15:2 compression-to-ventilation ratio vs continuous chest compressions. The 15:2 group had only 16 seconds/min of hand-off time (i.e., no compression). Neurologically intact survival was reported in two of 15 for the 15:2 group, vs 12 of 15 for the continuous chest compression group [11]. Yu et al. [12] studied time delay for AED waveform analysis. In swine with VF, return of spontaneous circulation (ROSC) was achieved in five of five among those who had a pause of 3 seconds vs zero of five for those with a pause of more
than 15 seconds. Even delays for applying rescue breaths were shown to be hemodynamically detrimental to swine receiving CPR [13].

During a resuscitation attempt, many factors detract from performance of chest compressions. Attaching the monitor, the pulse check, establishing an airway, establishing intravenous access, rhythm evaluation, medication administration, and ventilation are just some of the distractions from continuous chest compressions. These interruptions of chest compressions may decrease successful defibrillation and ROSC [14,15,18]. During EMS resuscitations, chest compressions were done for less than 50% of the resuscitation. In a study of first-responder AED use, hands-off time programmed by the AED accounted for 40% of the time the AED was applied to the patient [21]. The amount of hands-off time can also be related to the probability of ROSC [20]. Studies in Memphis and Hong Kong with similar findings have helped to add to the evidence of the importance of CPR [16*,17].

**Cardiac arrest**

Looking at the pathophysiology of no-flow cardiac arrest gives some answers as to why VF shocked after 2–3 minutes responds much better than VF shocked at 7–8 minutes. VF and cardiac arrest are much more than just electrical phenomena. The mechanical, metabolic, and electrical deterioration of the heart during prolonged VF is incompletely understood [4,18]. The oxygen supply deficit of the high-energy-requiring myocytes and the ensuing depletion of metabolic substrates contribute greatly to the circulatory demise. During the first 15–30 seconds after cardiac arrest, carotid and coronary artery blood flow drop precipitously. During this initial period, the intravascular volume redistributes into the venous and right-sided heart system. As the right side of the heart distends and the left side empties, a low-pressure gradient continues in providing some small amount of coronary and carotid flow. After this first 4–5 minutes, however, the left side of the heart empties and the flow stops [1,2]. It is during this initial 4–5 minutes, termed the electrical phase [3] by Weisfeldt and Becker, that the fibrillating heart is most responsive to electrical defibrillation. Once the left side of the heart empties and flow stops (the circulatory phase), the chance of restarting an empty, metabolically starved, fibrillating heart into an organized rhythm is remote [25].

Chest compressions restore some of the pressure gradient between the left and right sides of the heart, thus allowing the left side to fill and create some small but beneficial flow in the coronary and carotid arteries. CPR has been shown to provide about 30% of the normal cardiac output. In pigs, Steen [25] was able to produce coronary artery perfusion pressures of 12–18 mmHg with CPR after 6.5 minutes of induced VF (up from 0 mm Hg). Klouche et al. [4] had similar results from their swine experiments, with coronary perfusion pressures ranging from 9–28 mm Hg with mechanical chest compressions after 7 minutes of untreated VF. Videos of the swine heart during fibrillation and resuscitation show the empty left side of the heart being shocked into an organized sinus rhythm. With no blood to pump, however, and therefore no flow and no coronary perfusion pressure, clinically we have pulseless electrical activity. The left ventricle, even partially filled with blood from CPR, when defibrillated into an organized electrical rhythm, would enable a return of pulsatile flow and perfusion, returning the circulation to a self-sustaining state [25].

**Cardiopulmonary resuscitation first**

Based on the above pathophysiologic model of cardiac arrest, it is easy to understand why the results for the on-site providers, who had response times of less than 4 minutes, were so much better than those with average response times of greater than 6 minutes. This provides a structure for determining why performance of CPR would be beneficial during the circulatory phase prior to defibrillation. Does it work in practice?

Several studies of animals have shown significant benefit for the CPR first idea. Yakaitis [5] reported that after 5 minutes of VF, dogs that received 1 minute of CPR had an 80% resuscitation rate vs 30% of those who underwent defibrillation immediately after the 5-minute period of VF. In his study on dogs, Niemann [6] demonstrated that following 7.5 minutes of VF, a 20% rate of ROSC for dogs that underwent immediate defibrillation vs 60% ROSC for animals that had 5 minutes of CPR plus epinephrine prior to defibrillation [6]. Niemann also reported that of swine that had been resuscitated from 5 minutes of VF, those that had immediate defibrillation had 64% ROSC vs 95% for those that received 90 seconds of CPR preceding the defibrillation. [7*]. These studies provide significant physiologic evidence of the importance of CPR to ‘prime the pump’ prior to reorganizing the electrical activity.

In humans, the clinical data are, of course, not as precise, but they are still very promising for CPR first. There have been several studies of prehospital cardiac arrest and the impact of a CPR-first strategy (Table 1). A Swiss study compared outcomes of SCD after providing AED capabilities, decreasing defibrillation times from 15.6 minutes to 5.7 minutes. Outcomes worsened, however, with 1-year survival dropping from 17.9 to 9%. They concluded that their paramedics could not respond quickly enough to provide immediate defibrillation and that the CPR provided by the earlier BLS unit may have actually helped save more lives [8]. In Seattle, the addition of AEDs to the first responders did not improve outcomes, even though defibrillation times had dropped. One interpretation is that defibrillation was performed when the heart was empty. Based on the animal data above, the Seattle EMS protocol
Table 1. Recent papers evaluating a ‘delayed defibrillation’ approach

<table>
<thead>
<tr>
<th>Study</th>
<th>Type, n</th>
<th>Level of evidence</th>
<th>Intervention</th>
<th>Outcome, control</th>
<th>Outcome, experimental</th>
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</thead>
<tbody>
<tr>
<td>Niemann, et al.</td>
<td>Swine, 31</td>
<td>6</td>
<td>5 min of VF-1 min of CPR prior to defibrillation</td>
<td>64% ROSC (immediate defibrillation)</td>
<td>95% ROSC</td>
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<tr>
<td>et al. [31], 2000</td>
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<tr>
<td>Niemann, et al.</td>
<td>Canine, 28</td>
<td>6</td>
<td>7.5 min of VF-epi + CPR</td>
<td>21% ROSC (immediate defibrillation)</td>
<td>65% ROSC</td>
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<td>et al. [30], 1992</td>
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<tr>
<td>Cobb, et al.</td>
<td>Human (observational, prospective, population based), 1117</td>
<td>3</td>
<td>90 s of CPR prior to defibrillation</td>
<td>7% survival to hospital d/c (immediate defibrillation)</td>
<td>17% survival to hospital d/c</td>
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<tr>
<td>et al. 6*</td>
<td></td>
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<tr>
<td>Stotz, et al.</td>
<td>Retrospective chart review-before and after, 168</td>
<td>4</td>
<td>EMS defibrillation capable (emphasis shift from CPR to rapid defibrillation)</td>
<td>23.7% (average defibrillation at 15.6 min)</td>
<td>14.1% (average defibrillation at 5.7 min)</td>
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<td>et al. [32], 2003</td>
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<tr>
<td>Wik, et al.</td>
<td>Human (randomized controlled trial; subgroup analysis of response times &gt;5 mins), 200</td>
<td>2</td>
<td>3 min of CPR prior to defibrillation</td>
<td>2/41 (4%) survival to hospital d/c (immediate defibrillation)</td>
<td>14/41 (24%) survival to hospital d/c</td>
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<tr>
<td>et al. [33*], 2003</td>
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Level of Evidence, selected: Level 2 Randomized clinical trials with smaller or less significant treatment effects Level 3 Prospective, controlled, nonrandomized, cohort studies Level 4 Historical, nonrandomized, cohort, or case-control studies Level 5 Case series; patients compiled in serial fashion, lacking a control group Level 6 Animal studies or mechanical model studies CPR, cardiopulmonary resuscitation; EMS, emergency medical system; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

now provides 90 seconds of chest compressions prior to performing defibrillation. Again, comparing before and after implementation, the addition of 90 seconds of chest compressions improved overall survival from 24 to 30%, with 78% of the survivors having favorable neurologic status, up from 71% [6]. The biggest improvement came in patients who had a delay of greater than 4 minutes until defibrillation, increasing from 17 to 27%. In Norway,Wik et al. [9] performed a randomized controlled trial comparing the effects of a CPR-first strategy. Patients who had out-of-hospital VF were randomly assigned to receive either standard care with immediate defibrillation or 3 minutes of chest compressions prior to defibrillation. Although overall there was no benefit to the CPR strategy, a subgroup analysis of patients whose response times were longer than 5 minutes had ROSC of 58% compared with 38%, and there was a 1-year survival of 20 vs 4% in the immediate defibrillation group. These studies showed the potential benefit of the application of a CPR-first strategy for patients in prolonged VF.

The question that is raised, however, is how to determine which patients are in the ‘electrical phase’ and need immediate defibrillation and which are in the ‘circulatory phase’ and would benefit from some period of CPR prior to attempting defibrillation. The human studies performed show immediate defibrillation to be beneficial in cases in which time to defibrillation is less than approximately 3 minutes. The precise time of onset of OOH-CA is unknown in the vast majority of cases, however.

Bystander CPR, if performed properly, has been shown to be beneficial [10,11]. In a recently published abstract, Vilke et al. [12] report significantly higher survival in patients with down times of 4–10 minutes if they received bystander CPR. Even CPR performed by untrained laypersons given instructions by the EMS dispatcher has been investigated [13,14]. The quality of bystander CPR and therefore its benefit can be highly variable, however. Witness reports of time intervals are often unreliable and many patients have un witnessed arrest. The ability to determine the phase of cardiac arrest and predictability of defibrillation response based upon the electrical pattern of the fibrillation waveform have been examined in animal models and humans. Amman et al. [15] retrospectively compared data to determine this predictability based on a combination of fibrillation wave mean frequency and amplitude, with promising results. With only a single 5-second waveform reading of waveform angular velocity, Sherman et al. [16*] were able to identify with a 90% sensitivity the swine that had less than 5 minutes of VF vs those that had more than 5 minutes of VF. In an evaluation of the human VF waveforms from the previously discussed randomized, controlled trial, Effestol [17] reported that several predictors of ROSC defibrillation success were improved after 3 minutes of CPR.

**Conclusion**

Rapid defibrillation is a mantra that pervades nearly all EMS organizations, as an extrapolation from well-demonstrated immediate defibrillation success. Since the time intervals for most OOH-CA victims usually produce delayed defibrillation, performing CPR first may refill the left ventricle and optimize the chances for defibrillation, allowing development of a pulsatile rhythm. Any change to the current emergency-and-rescue culture regarding defibrillation would require additional, compelling data from a formal hypothesis-testing trial. A large, randomized, multicenter, hypothesis testing study is needed to confirm or refute the reproducibility and generalizability of...
a CPR-first strategy. We envision that future cardiac arrest guidelines will include these strategies, as well as techniques that evaluate information ‘hidden’ in the VF waveform, that would guide the rescuers to perform immediate shock or optimized CPR for a period until defibrillation would be expected to produce ROSC and increased survival.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
* of special interest
** of outstanding interest


This paper discusses the difficulty in statistical analysis of cardiac arrest, determining a denominator is difficult because of different interpretations of the definition or inclusion criteria for a cardiac arrest.


This study shows the benefit and safety of layperson use of AEDs throughout the community.


The authors retrospectively evaluated the VF waveforms from the Wik randomized, controlled study and showed that 3 minutes of CPR created a VF waveform with a higher probability of successful defibrillation.