WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)  
Steven M. Bradley

Date Submitted for review: 2 February 2010

Clinical question.
"In adult cardiac arrest due to VF or pulseless VT (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of any specific defibrillation strategy (I) compared with standard management (or other defibrillation strategy) (C), improve outcomes (eg. termination of rhythm, ROSC, survival) (O)?"

Is this question addressing an intervention/therapy, prognosis or diagnosis: Therapy

State if this is a proposed new topic or revision of existing worksheet: New

Search strategy (including electronic databases searched).
PubMed ("heart arrest" OR "cardiopulmonary resuscitation" as MESH (headings) OR "resuscitation" as text word (all fields)) AND ((("electric countershock/therapy" OR "electric countershock/methods" OR "electric countershock/standards" as MESH (headings)) OR ("defibrillat*protocol" OR "defibrillat* strategy" OR "defibrillat* energy" as text words (all fields)) OR ("electric countershock" OR "defibrillators" AND "clinical protocols" as MESH(headings))).
EMBASE ("resuscitation" text word (all fields) OR “cardiac arrest” text word (all fields) OR “heart arrest” subject heading) AND (“defibrillat*” textword (all fields) OR “defibrillator” subject heading OR “defibrillation” subject heading) AND (“protocol” text word (all fields) OR “strateg*” text word (all fields) OR “clinical protocols” subject heading))
Cochrane Library (including Cochrane Database of Systematic Reviews and Cochrane Register of Controlled Trials) ("heart arrest" OR "cardiopulmonary resuscitation") AND ("electric countershock" OR "defibrillators") as MESH terms
AHA EndNote Master library “defibrill*” AND “heart arrest” as Keywords.

Each of these searches was manually reviewed (title and abstract first and full article if necessary) to identify articles in which a strategy of defibrillation was compared to standard management or other defibrillation strategy. In addition, all citations listed in key articles were reviewed.

State inclusion and exclusion criteria
Inclusion of cardiac arrest studies or cardiac arrest models with evaluation of defibrillation energy or serial shocks.
Exclusion of non-cardiac arrest studies (eg. cardioversion of atrial fibrillation, supraventricular tachycardia) or non-cardiac arrest animal models (eg. exsanguinations, great vessel occlusion [x], carotid artery occlusion [y]), pre-arrest [z] or during arrest cooling [a].

Number of articles/sources meeting criteria for further review:
Search strategy identified the following number of sources: PubMed 903 (29 Sept 2009), EMBASE 394 (29 Sept 2009), Cochrane Library 254 (29 Sept 2009), AHA EndNote Master library 257 (10 Sept 2008).
Of these, review or title and abstract resulted in 188 studies that met criteria for further review. Of these, 53 studies were pertinent to the clinical question of high compared to lower starting defibrillation energy, 42 studies pertinent to the clinical question of biphasic compared to monophasic waveform defibrillation, 8 studies pertinent to the clinical question of multiphasic compared to biphasic waveform defibrillation, and 6 studies pertinent to the question of one shock compared to three stacked shocks. Of the 53 studies pertinent to the question of high compared to lower starting defibrillation energy, 2 were LOE 1 (RCTs), 4 were LOE 2 (non-randomised, concurrent controls), 1 was LOE 3 (retrospective controls), 18 were LOE 4 (no controls), and 28 were LOE 5 (not directly related or animal studies). Of the 42 studies pertinent to the question of biphasic compared to monophasic waveform defibrillation, 5 were LOE 1 with two studies reporting on the same patients, 3 were LOE 3, 10 were LOE 4, and 24 were LOE 5. Of the studies pertinent to the question of high compared to lower starting defibrillation energy, 2 were LOE 1, 4 were LOE 2, 18 were LOE 4, and 28 were LOE 5. Of the 8 studies pertinent to the question of multiphasic compared to biphasic defibrillation waveform, all 8 were LOE 5. Of the 6 studies pertinent to the question of one shock compared to three stacked shocks, 1 was LOE 2, 2 were LOE 3, and 3 were LOE 5.
## Summary of evidence – High starting energy vs Low starting energy

### Evidence Supporting Clinical Question

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<tr>
<th>Good</th>
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|      |      | Morgan 1984, E  
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|      |      | Higgins 2000, E  |
|      |      | Clark 2001, E  
         |      | Geddes 1974, E  
         |      | Jones 1990, E  
         |      | Lerman 1987, E  
         |      | Zhang 2003, E  |

### Evidence Neutral to Clinical Question

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|      |      | Stiell 2007, ABCDE  
         |      | Weaver 1982, ACE  |
|      |      | Gascho 1979, BCE  
         |      | Kerber 1983, E  
         |      | Walsh 2004, E  |
|      |      | Jakobsson 1989, C  
         |      | Morgan 1984, BC  |
|      |      |      |
|      |      | Carpenter 2003, ABCE  
         |      | Freeman 2008, ACE  
         |      | Heavens 1998, BCE  
         |      | Hess 2008, ADE  
         |      | Kudenchuk 2006, ABCDE  
         |      | Morrison 2005, ABCDE  
         |      | van Alem 2003, E  |
|      |      | Gliner 1998, AE  
         |      | Hess 2004, ABCE  
         |      | Schneider 2000, ABCDE  
         |      | White 2002, ABCDE  
         |      | White 2004, ABCE  
         |      | White 2005, ABCE  |
|      |      | Poole 1997, E  
         |      | Stothert 2004, E  
         |      | White 1997, E  
         |      | White 2001, ABCE  |
|      |      |      |
|      |      | Bain 2001, E  
         |      | Bardy 1995, E  
         |      | Bardy 1996, E  
         |      | Berg 2005, E  
         |      | Clark 2002, E  
         |      | Greene 1995, E  
         |      | Mittal 1999, E  
         |      | Niemann 2003, AE  
         |      | Tang 2006, AE  
         |      | Walcott 2002, A  
         |      | Walker 2003, E  
         |      | Xie 1997, AB  |
|      |      | Rossano 2006, C  
         |      | Szili-Torok 2002, E  |
|      |      |      |
|      |      | Higgins 2004, E  
         |      | Killingsworth 2002, E  
         |      | Niemann 2000a, AE  
         |      | Niemann 2000b, E  
         |      | Walcott 1998, E  
         |      | Yamanouchi 1999, E  |

### Levels of evidence

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
- **D** = Intact neurological survival
- **E** = Other endpoint
- *Italics* = Animal studies

1 – overlapping patients
### Evidence Opposing Clinical Question

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| **Good**          |   |   |   |   | Carpenter 2003, E  
                      |   |   |   |   | Freeman 2008, E |
| **Fair**          | Morrison 2005, E  
                      | Schneider 2000, ADE  
                      | Koster 2006, E³  
                      | van Alem 2003, E³ | Gliner 1999, E |
| **Poor**          |   |   |   |   |   |

**Summary of evidence – Biphasic vs Monophasic**

- **Evidence Supporting Clinical Question**
  - Good: Carpenter 2003, E
  - Fair: Morrison 2005, E, Schneider 2000, ADE
  - Poor: Jones 1990, E

**Evidence Opposing Clinical Question**

- Fair: No evidence
- Poor: No evidence

**Level of evidence**

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<td>( \text{Level of evidence} ) (D = Intact neurological survival)</td>
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<td>Morrison 2005, ABCD Schneider 2000, BC</td>
<td>Fair (B = Survival of event)</td>
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### Summary of evidence – Multiphasic vs Biphasic Defibrillation

#### Evidence Supporting Clinical Question

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*Italics = Animal studies*
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**Summary of evidence – One vs Three Stacked Shocks**

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**Reviewer’s Final Comments and Assessment of Benefit / Risk:**

**Discussion:**

This worksheet seeks to determine if the use of any specific defibrillation strategy improves outcomes of cardiac arrest. Broadly, this could be considered to include questions regarding defibrillation energy (escalating compared to fixed dose energy; high compared to low starting energy dose), defibrillation waveform (biphasic compared to monophasic; multiphasic compared to biphasic), paddle/pad size and orientation, defibrillation timing in the resuscitation sequence (one shock compared to three stacked shocks; CPR prior to defibrillation, prediction of defibrillation success to guide defibrillation timing), and impact of pharmacologic therapies on defibrillation efficacy. Many of these topics are considered in other worksheets (escalating compared to fixed dose energy defibrillation ALS-E-032; paddle/pad size, orientation and position ALS-E-030; CPR prior to defibrillation BLS024; technique for predicting likelihood of defibrillation success ALS-D&P-015; pharmacologic therapies ALS-D-023, ALS-D-024, and ALS-D-025). The current worksheet thus focuses on the questions of high energy compared to low starting defibrillation energy, biphasic compared to monophasic defibrillation waveform, multiphasic compared to biphasic defibrillation waveform, and one shock compared to three stacked shocks.

### Higher starting energy compared to lower starting energy for defibrillation with biphasic waveform:

- This question seeks to determine if a higher starting energy biphasic defibrillation improves outcome compared to lower starting energy biphasic defibrillation.
- The first human comparison of different biphasic energy levels was conducted by Walsh et al. This was a nonrandomized study of 78 patients with either in-hospital or out-of-hospital cardiac arrest. Energy dosing regimen depended on study site. One site used fixed energy biphasic defibrillation (150-150-150J) while the other site used an escalating energy protocol with a lower starting energy dose (100-150-200J). After first shock, successful termination of ventricular fibrillation at 5 seconds post-shock was seen in 46/79 (58%) patients treated with 100J energy shock and 61/95 (64%) treated with 150J energy shock (p=">NS”). Among patient requiring 3 shocks for termination of ventricular fibrillation, a greater proportion achieved successful defibrillation in the lower starting dose with escalating dose protocol. This suggests there is no benefit to higher starting energy for defibrillation protocol. This study was limited by its nonrandomized design, violations of energy protocol in >30% of patients treated with escalating dose protocol, lack of adjustment for differences in baseline characteristics and adjunctive therapies, and lack of data regarding return of spontaneous circulation or survival to hospital discharge.
- The study by Stiell et al. added significantly to our knowledge regarding energy protocols for biphasic defibrillation. This was a randomized controlled trial of 221 patients with out-of-hospital cardiac arrest due to ventricular fibrillation. This study compared lower dose fixed energy biphasic defibrillation (150-150-150J) to higher dose escalating energy biphasic defibrillation (200-300-360J). First shock successfully terminated ventricular fibrillation at 5 seconds post-shock in 99/114 (86.6%) treated with lower energy biphasic defibrillation and 95/107 (88.8%) treated with higher energy biphasic defibrillation (p=0.81). A similar proportion achieved organized rhythm at 60 seconds after first shock when treated with lower energy (43/112, 38.4%) or higher energy (36/98, 36.7%) biphasic defibrillation (p=0.92). Similar to the results of Walsh, a higher proportion achieved termination of VF and organized first rhythm with escalating dose defibrillation when more than one shock was required. This study further suggests there is no benefit to higher starting energy for defibrillation of cardiac arrest.
- Several randomized controlled trials and cohort studies have compared low-dose biphasic defibrillation to higher energy monophasic defibrillation. While these studies do not permit a comparison of biphasic defibrillation at different energies, they do provide an estimate of defibrillation efficacy with first shock. In the randomized controlled trial by Schneider et al., 92% (44/48) of ventricular fibrillation was terminated with first biphasic shock at 150J. A randomized controlled trial by Kudenchuk et al. demonstrated termination of VF after first shock in 65/74 (88%) with return of organized rhythm in 25/74 (34%). In the randomized controlled trial by Morrison et al., an organized rhythm was observed in 35/146 (24.0%) treated with biphasic waveform at 120J. Cohort studies by Carpenter et al., Gliner et al., Hess et al., and White et al. suggest successful termination of ventricular fibrillation after low-dose biphasic defibrillation ranges from 86-92%. When using the electrical endpoint of termination of ventricular fibrillation, these studies suggest there is little room for improvement with a higher starting energy. However, it remains important to tie these electrical endpoints to improved survival.

**Statistical Summary of Critical Studies:**

**Summary of Stiell 2007, Walsh 2004**

- Randomized, blinded clinical trial of a fixed lower-energy biphasic (150-150-150J) and an escalating higher-energy biphasic (200-300-360J) defibrillation protocol at 3 sites. 2002-2005. 256 assessed, 221 enrolled (26 excluded after blinded review determined asystolic at time of defibrillator shock, 7 excluded due to incomplete data, 2 traumatic arrests excluded)
- Termination of VF and organized rhythm (defined as at least two consecutive QRS complexes separated by no more than 5 seconds) within 60 seconds after first shock 38.4% with low-energy vs 36.7% with higher-energy biphasic defibrillation (p=0.92). Among patients requiring more than one shock, termination of VF was 24.7% in fixed low-energy vs 36.6% in escalating higher-energy biphasic defibrillation (absolute difference 11.9%, 95% CI 1.2 to 24.4%; NNT = 8).
Summary of Walsh 2004:

- Successful defibrillation (defined as cessation of ventricular fibrillation for ≥5 seconds) for episodes of ventricular fibrillation was the same after the first shock (46/79 escalating dose (58%) vs 61/95 fixed dose (64%)) and second shock (65/79 escalating dose (82%) vs 74/95 fixed dose (78%)).
- A higher proportion were successfully defibrillated with escalating dose defibrillation when three shocks were required (73/79 escalating dose (92%) vs 79/95 fixed dose (83%)) (absolute difference 9%, p = 0.029, NNT = 11).

Biphasic compared monophasic waveform transthoracic defibrillation:

- This question seeks to determine if a biphasic defibrillation improves outcome compared to monophasic defibrillation waveform. The first human studies of transthoracic defibrillation with biphasic waveforms were performed at the time of ICD placement. A meta-analysis conducted by Faddy et al. summarized the results of these studies. Biphasic and monophasic waveforms had similar overall efficacy in termination of VF, but biphasic waveforms reduced the risk of asystole or persistent VF after the first shock by 91% (RR=0.19, 95% CI 0.06-0.60).
- The first randomized clinical trial of biphasic waveform compared to monophasic waveform was conducted by Schneider et al and compared monophasic waveform of energy 200 to 360J to biphasic waveform of 150J within 4 EMS systems. The study included 246 patients with out-of-hospital cardiac arrest. Randomization occurred via daily exchange of defibrillators. The primary endpoint of termination of VF within 3 shocks was achieved by a greater proportion treated with biphasic 150J (54/54, 98%) than with monophasic 200 to 360J (42/61, 69%, p<0.0001). Additionally, ROSC was achieved in 76% of patients after biphasic shocks compared to 54% of those treated with monophasic shocks (p=0.01). Despite improvements in short-term outcomes, there were no differences in survival to discharge. Among survivors to hospital discharge, 87% treated with biphasic shocks had good cerebral status compared with only 53% among patients resuscitated with monophasic shocks.
- A randomized clinical trial conducted by van Alem et al. compared biphasic and monophasic waveform defibrillation with the same energy protocol (200-300-360J) for treatment of out-of-hospital cardiac arrest. Randomization occurred via random relocation of AEDs on a 4 month basis. A total of 217 patients were evaluated with AED, with shock being advised in 123 and delivered to 120. Analysis was restricted to those receiving shock and demonstrated the primary endpoint of organized rhythm at 60 seconds post-shock was more frequent among those treated with biphasic shocks (35/51, 69%) than with monophasic defibrillation (31/69, 45%; p=0.01). There was no difference in ROSC, survival to admission, or survival to discharge. The results of this trial were republished by Koster et al. with multiple logistic regression suggesting the odds of organized rhythm at 60 seconds post-shock were 4 fold greater after biphasic shock than monophasic shock.
- Another randomized clinical trial of biphasic waveform compared to monophasic waveform in the treatment of out-of-hospital cardiac arrest was conducted by Morrison et al. This study randomized to monophasic waveform with energy protocol 200-300-360J or biphasic waveform 120-150-200J. Randomization occurred at the level of the AED. A total of 429 validated cases were included in the study. Among patients shockable on arrival of EMS, the primary outcome of organized rhythm at 5 seconds post-shock was achieved by a greater proportion treated with biphasic waveform (45/86, 52.3%) than monophasic waveform (28/83, 33.7%, p=0.01). Similarly, organized rhythm was achieved in a greater proportion of patients treated with biphasic waveform among patients shockable during resuscitation for out-of-hospital cardiac arrest. No differences in ROSC, survival of event, survival to hospital discharge, or cerebral perfusion category at discharge were observed between treatments.
- The clinical trial by Kudenchuk et al. of biphasic compared to monophasic waveform for transthoracic defibrillation of out-of-hospital cardiac arrest randomized waveform at the patient level and blinded responders to the waveform used. Additionally, caution was taken to eliminate differences in hands-off AED analysis periods and AED interface that could have potentially confounded the results of other randomized trials. This study randomized 168 patients to either monophasic defibrillation or biphasic defibrillation with the same energy protocol (200-300-360J). The defibrillation waveform provided throughout resuscitation did not match the AED randomized waveform in 80 (48%) of patients randomized to monophasic waveform and 68 (40%) of those randomized to biphasic waveform. Patients requiring more than 1 shock who had waveform mismatch were excluded from the analysis. There was no difference in the primary outcome of admission to hospital with a perfusing rhythm between therapies (monophasic n=58, 73% vs biphasic n=52, 76%; p=0.58). Similar proportions treated with monophasic or biphasic waveforms achieved termination of VF with first shock (82% and 88% respectively, p=0.33), organized rhythm (26% and 34% respectively, p=0.30), and ROSC (20% and 24% respectively, p=0.51). The strengths of this study include randomization at the patient level, complete blinding to waveform provided, and elimination of differences in hands-off time and AED interface.
Retrospective cohort studies by Carpenter et al. and Freeman et al. further suggest that biphasic waveforms are associated with improved short term outcomes such as termination of VF or organized rhythm after defibrillation, but no improvements in survival to hospital discharge were observed with biphasic defibrillation.

A study by Reddy et al. at the time of ICD placement suggested less myocardial injury post-shock as measured by ST-segment changes on ECG with biphasic compared to monophasic transthoracic defibrillation. Animal model studies by Tang et al. also suggest less myocardial dysfunction following biphasic defibrillation compared to monophasic defibrillation.

Together these randomized and observational studies suggest a consistent trend of greater termination of VF, return of organized rhythm, and ROSC with biphasic defibrillation for out-of-hospital cardiac arrest compared to monophasic defibrillation. These short-term improvements have not been associated with improved survival, but data from Schneider et al. suggests biphasic defibrillation is associated with better neurologic status among survivors. Together, these data support use of biphasic defibrillation over monophasic defibrillation. Meta-analysis of available randomized trials may help clarify the effect of biphasic defibrillation on survival compared to monophasic defibrillation.


**Summary of Schneider 2000:**
- Randomized (daily at EMS unit level) clinical trial of fixed energy biphasic waveform (150J) and monophasic waveform of 200 or 360J for treatment of OHCA. 1996-1998. 338 enrolled, 246 with arrest of cardiac etiology and not witnessed by EMS personnel and randomized. No statistical differences in baseline characteristics or EMS-response characteristics.
- Greater termination of VF (≥ 5 seconds) within 3 shocks with biphasic (46/48, 92%) compared to monophasic (49/67, 73%, p=0.002). Biphasic also resulted in a larger proportion achieving ROSC (81% vs 52%, p=0.001) and survival to hospital admission (69% vs 46%, p=0.02).
- No evidence of improved survival to hospital discharge after biphasic defibrillation (16/48, 33%) compared to those treated with monophasic waveform (18/67, 27%, p=0.45). Among those who survived to discharge, cerebral performance status was good in 87% of patients treated with biphasic waveform compared to 53% treated with monophasic waveform (p=0.04).
- Limitations included randomization on the basis of date, not blinded to EMS provider, multiple models of AED with potential confounding on interface and delays to defibrillation.

**Summary of van Alem 2003:**
- Randomized (every 4 months at responder level) clinical trial of biphasic waveform and monophasic waveform with the same energy protocol (200-300-360J) for treatment of OHCA. 2000-2002. Total of 217 patients evaluated with AED, shock being advised in 123 and delivered to 120. Analysis restricted to those receiving shock.
- Primary endpoint of organized rhythm at 60 seconds post-shock was more frequent among those treated with biphasic shocks (35/51, 69%) than with monophasic defibrillation (31/69, 45%; p=0.01). There was no difference in ROSC, survival to admission, or survival to discharge.
- Limitations included randomization at the AED level, no evidence of confounding as assessed by logistic regression.

**Summary of Morrison 2005:**
- Randomized (at AED level) clinical trial of biphasic waveform (120-150-200J) and monophasic waveform (200-300-360J) for the treatment of OHCA. Enrolled 538, with 429 validated cases.
- Among patients shockable on arrival, primary endpoint of organized rhythm at 5 seconds post-shock after one to three shocks achieved by a greater proportion of patients treated by biphasic waveform (45/86, 52.3%) than monophasic waveform (28/83, 33.7%, p=0.01).
- Among patients shockable during resuscitation, primary endpoint of organized rhythm at 5 seconds post-shock after one to three shocks achieved by a greater proportion of patients treated by biphasic waveform (90/163, 55.2%) than monophasic waveform (66/149, 44.3%, p=0.05).
- No differences in ROSC, survival of event, survival to hospital discharge, or cerebral perfusion category at discharge were observed between treatments.
- Limitations include randomization at level of AED resulting in 80% compliance of randomization at patient level, differing energy protocols, and analysis did not adjust for blocked randomization.

**Summary of Kudenchuk 2006:**
- Randomized (at the patient level), blinded, clinical trial of biphasic waveform and monophasic waveform with the same energy protocol (200-300-360J) for the treatment of OHCA. 862 enrolled, 168 randomized. Mismatch between randomized waveform and subsequent waveform during resuscitation in 80 (48%) randomized to monophasic and 68 (40%) randomized to biphasic. Patients with >1 shock and mismatched waveform excluded from analysis.
- No difference in the primary outcome of admission to hospital with a perfusing rhythm between therapies (monophasic n=58, 73% vs biphasic n=52, 76%; p=0.58).
- Monophasic and biphasic waveforms resulted in similar termination of VF with first shock (82% and 88% respectively, p=0.33), organized rhythm (26% and 34% respectively, p=0.30), and ROSC (20% and 24% respectively, p=0.51).
The strengths of this study include randomization at the patient level, complete blinding to waveform provided, and elimination of differences in hands-off time and AED interface.

**Multiphasic compared to biphasic waveform transthoracic defibrillation:**
- There are no human studies to date evaluating multiphasic defibrillation waveforms compared to biphasic (or monophasic) defibrillation waveforms. Several animal studies have evaluated defibrillation thresholds for triphasic truncated exponential waveforms compared to biphasic truncated exponential models in animal models. Most of these studies suggest similar defibrillation efficacy between waveforms, but are hampered in their application to cardiac arrest by short duration of VF (<30 seconds), ICD testing, or open-chest animal models. Animal model studies by Zhang suggest greater defibrillation efficacy (termination of VF at 5 seconds post-shock) at energies <90J and less post-shock myocardial dysfunction with triphasic waveforms compared to biphasic waveforms.

Another animal model study by Zhang suggested higher defibrillation efficacy with quadriphasic waveform compared to triphasic waveform in animal models with higher transthoracic impedance, but no difference in post-shock myocardial dysfunction was observed.

**One compared to Three Shock Protocols:**
- Traditionally, defibrillation shocks were provided in stacked series of three shocks in the attempt to terminate ventricular fibrillation or ventricular tachycardia as quickly as possible. However, animal studies have indicated that interruptions or delays in CPR immediately before defibrillation, as would be expected with stacked shocks, results in lower likelihood of survival.
- Two pre-post design studies in humans have evaluated a one shock defibrillation protocol compared to a three shock defibrillation protocol. Both studies incorporated additional changes to CPR protocol, making an assessment of the effect size attributable to the change in defibrillation protocol challenging.
- In the study by Rea et al., a cohort of patients with out-of-hospital cardiac arrest were treated with single shock defibrillation without rhythm reanalysis or postdefibrillation pulse check. Additionally, the period of cardiopulmonary resuscitation between rhythm analysis was extended to 2 minutes. This group was compared to an historical control. Patients treated during the intervention period were more likely to survive to hospital discharge (45.5% vs 32.8%, p<0.05) and be discharged to home (36.6% vs 25.6%, p<0.05). The intervention and historical groups were similar in patient and EMS-response characteristics. It remains unclear how much of the observed effect is related to the protocol changes for post-shock CPR as opposed to single shock.
- Bobrow et al. extended upon these findings in their pre-post analysis of minimally interrupted resuscitation. In this study, a cohort of patients was treated with 200 uninterrupted chest compressions, rhythm analysis with a single shock, 200 post-shock chest compressions without rhythm reanalysis, early epinephrine, and delayed endotracheal intubation. When compared to an historical control, survival to hospital discharge increased from 4/218 (1.8%) during the control period to 36/668 (5.4%) with the intervention. Similar to the study by Rea et al., multiple interventions were part of the protocol change. Thus, the effect size of single shock compared to three shocks alone cannot be determined.

**Statistical summary of critical studies: Rea 2006, Bobrow 2008**

**Rea 2006:**
- Observational pre-post design comparing protocol change including single shock defibrillation, elimination of post-shock pulse check and rhythm reanalysis, and extension of post-shock compression period to 2 minutes to historical control period that included stacked shocks in protocol in treatment of OHCA due to VF. Intervention period 2005-2006, control period 2002-2004. Proportion meeting inclusion criteria for intervention period (134/869, 15.4%) and control period (374/2255, 16.6%) were similar.
  - Primary outcome of survival to hospital discharge achieved in a greater proportion of patients treated during the intervention period (45.5% vs 32.8%, p=0.008).
  - The proportion of patients discharged to home was greater among those treated during the intervention period (36.6% vs 25.6%, p<0.05).
  - The intervention and historical groups were similar in patient and EMS-response characteristics and adjustment for covariates did not change the results.
  - Several protocol changes were implemented during the intervention period. The effect size directly attributable to single shock protocol compared to stacked shocks cannot be determined.

**Bobrow 2008:**
- Observational pre-post design comparing protocol change to include 200 uninterrupted chest compressions, rhythm analysis with a single shock, 200 post-shock chest compressions without rhythm reanalysis, early epinephrine, and delayed endotracheal intubation to historical control period in treatment of OHCA. Intervention period – Site #1 2005-2007, Site #2 2006-2006. Control period – six months 2005. 1243 enrolled, 886 met inclusion criteria (218 control and 668 intervention).
- Primary outcome of survival to hospital discharge achieved in a greater proportion of patients treated during the intervention period (5.4% vs 1.8%, multiple logistic regression OR 3.0, 95% CI 1.1-8.9).
<table>
<thead>
<tr>
<th>REVIEWER’S CONFLICTS OF INTEREST:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steven M. Bradley – Internist/Cardiology Fellow.</td>
</tr>
<tr>
<td>No intellectual or commercial conflicts. Fellowship</td>
</tr>
<tr>
<td>supported by VA HSR&amp;D Post-MD Fellowship</td>
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</tbody>
</table>

**Acknowledgements:**
Graham Nichol for his mentorship in preparation of this worksheet.
Citation List

Higher Starting Energy Compared to Lower Starting Energy for Biphasic Defibrillation


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospectively randomized non-blinded comparison of monophasic (escalating 200-300-360J or fixed 360J) versus biphasic (escalating 200-300J or fixed 300J) transthoracic defibrillation for termination of VF (supraventricular or paced rhythm at 5 sec). Duration VF=10sec. N=118.
First shock successful in 100% of patients treated with biphasic waveform regardless of energy level.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospectively randomized and blinded to two energy levels of truncated biphasic transthoracic (115J or 130J) and monophasic damped sine waveform (200J). N=30.
For each transthoracic pulse, the percent defibrillation efficacy was 97%.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospective, randomized, blinded study comparing first shock efficacy of monophasic (200J or 360J) compared to biphasic (115 or 130J) transthoracic defibrillation. N=294.
First shock effectively terminated VF in 86/97 (89%) treated with 115J biphasic , 144/167 (86%) treated with 130J biphasic, 143/166 (86%) treated with 200J monophasic, and 80/83 (96%) treated with 360J monophasic. Differences in efficacy did not achieve statistical significance.


LOE 5 (animal), good, neutral. Prospective randomized comparison of escalating biphasic transthoracic defibrillation at a pediatric (50-75-86J) or adult (200-300-360J) energy dosage in a piglet model. N=16
Pediatric dose less effective at termination at first shock (pediatric 4/16 vs adult 12/16, p<0.005) and second shock (pediatric 11/16 vs adult 16/16, p=0.01). All piglets achieved ROSC within 3 shock sequence. Greater myocardial damage (enzymes and EF) with adult dosages.
Suggests that earlier defibrillation may be achieved with a higher starting energy, but must be balanced against possibility for greater post-shock myocardial dysfunction.


LOE 4, good, neutral. OHCA, retrospective cohort, BTE (fixed 150J and escalating 150-200-360J) vs MDS (150-200-360J) vs MTE (150-200-360J),N=366.
First shock efficacy:
BTE 94/105 (89.5%), MDS 162/193 (83.9%), MTE 43/68 (63.2%).
No comparison of biphasic waveform defibrillation at different starting energies.


LOE 5 (animal), poor, supportive. Prospective study evaluating monophasic and biphasic defibrillation waveforms ranging from 7 to 100J energy. Waveform and energy applied in random order to piglets of varying size to model infant and child. N=35
Termination of VF increased with increasing energy, with biphasic achieving >80% termination of VF by 20J in infant model and 30J in child model; monophasic required 50J in infant and 70J in child to achieve similar rates.


LOE 5 (animal), good, neutral. Prospective randomized evaluation of monophasic and biphasic shocks at five energy levels (70, 100, 200, 300, and 360J) in each animal, N=13. Duration of VF 15 seconds.
Defibrillation success with biphasic waveform increased to a maximum success rate at 100J with no further success at higher energies.

LOE 3, fair, neutral. OHCA, retrospective cohort, low-energy (130-130-180J) pulsed biphasic waveform compared to historical controls. Similar effectiveness of defibrillation with low-energy first shock compared to historical controls. Lower survival to hospital discharge compared to historical controls attributed to differences in witnessed arrest and receipt of bystander CPR.


LOE 4, good, neutral. OHCA, retrospective cohort, MTE vs BTE, 2000-2004 (MTE 2000-2002, BTE 2002-2004), N=485. More defibrillations required with monophasic defibrillation to achieve ROSC compared to BTE (3.5 vs 2.6, p=0.015). No difference observed in ROSC, survival to discharge, or discharge to home between MTE and BTE.


LOE 2, poor, neutral. IHCA, prospective cohort, monophasic defibrillation categorized into <80J, 81-160J, 161-240J, >241J; 1975-?, N=88. Trend toward less successful defibrillation after first shock (defined as any rhythm other than VF) when first shock energy >240J.


LOE 5 (animal), poor, supportive. Prospective study of defibrillation threshold defined by energy and peak current across a range of animals of varying weight. Increasing animal weight associated with increase defibrillation threshold as defined by energy.


LOE 4, fair, neutral. OHCA, retrospective, cohort. Biphasic fixed energy (150J) defibrillation. 1996-1998. N=100 Successful termination of VF with 1st shock 86%. No comparison of biphasic waveform defibrillation at different starting energies, thus considered case series for LOE.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospective, randomized evaluation of monophasic (200J) vs biphasic (200J) transthoracic defibrillation. N=171. Successful termination of VF with first shock: biphasic defibrillation 81/93 (97.6%); monophasic defibrillation 75/88(85.2%) (p=0.005). No comparison of biphasic waveform defibrillation at different starting energies.


LOE 4, good, neutral. OHCA, retrospective cohort, regression analysis to identify factors associate with successful rhythm conversion. 1991-1994, 436 OHCA with VF, 310 met inclusion for analysis. All treated with dampened sinusoidal waveform 200-200-360J. Successful termination of VF with first shock in 79/310 (25.5%). No comparison of biphasic waveform defibrillation at different starting energies, thus considered case series for LOE.


LOE 4, fair, neutral. OHCA, retrospective cohort of VF treated by police or firefighters with biphasic (150-150-150J) AED. 1996-2003. N=67. Successful termination of VF with first shock in 62/67 (92.5%) No comparison of biphasic waveform defibrillation at different starting energies, thus considered case series for LOE.


LOE 4, good, neutral. OHCA, retrospective cohort of patients treated with fixed low-dose biphasic AED. 1996-2007, N=103. Successful termination of VF with first shock in 93/101 (92.1%) No comparison of biphasic waveform defibrillation at different starting energies, thus considered case series for LOE.

LOE 5 (at time of ICD), good, supportive. Lab at time of ICD testing, randomized, prospective trial of monophasic (200J) compared to biphasic (130J or 200J) for transthoracic defibrillation. Duration of VF=19 seconds. N=115. First shock effectively terminated VF. Monophasic 200J - 61/68 (87.9%, 95% CI 79.9-95.8%); Biphasic 130J – 39/47 (83%, 95% CI 69.2-92.4%); Biphasic 200J – 39/39 (100%, 95% CI 91-100%). No significant difference in post-shock hemodynamic quantities.


LOE 5 (at time of ICD or EP testing), poor, neutral. Lab at time of ICD or EP testing, evaluation of biphasic (150J) waveform for transthoracic defibrillation compared to an historic control. Duration of VF=16 seconds. N=96. Biphasic 150J successfully terminated VF in 97.4% with first shock and successive fixed dose biphasic shocks effectively terminated VF in remaining two patients.


LOE 2, poor, supportive C, neutral BE. OHCA, retrospective, cohort of monophasic defibrillation of fixed energy (200J or 360J) or escalating energy (200J to 360J). Higher proportion of patients treated with fixed high energy (n=11, 7%) survived to discharge compared to low energy (n=3, 2%) or escalating (n=2, 4%) but no statistical test of significance. No adjustments undertaken for differences in baseline or EMS-response characteristics.


LOE 5 (animal), poor, supportive. Prospective study of defibrillation threshold with increasing duration of VF (5 to 30 sec) in an isolated rabbit heart model. Energy required for defibrillation with either waveform increased with duration of VF. Energy level required for defibrillation lower with biphasic pulse at all time points.


LOE 2, fair, neutral. IHCA, retrospective, cohort, monophasic defibrillation comparing defibrillation efficacy of starting energies. Similar defibrillation efficacy seen for <200J and 300 to 400J starting energies (56% vs 58%, p=NS). No difference in successful defibrillation with escalation related to starting energy (87% vs 89%).


LOE 5 (animal), poor, neutral. Prospective study of biphasic defibrillation up to 360J with adult or pediatric sized patches in a piglet model. N=10 No increase in defibrillation efficacy with higher energy shocks. Only transient myocardial dysfunction observed with higher energy shocks.


LOE 4, good, neutral. OHCA, prospective randomized (at the level of EMS unit) clinical trial of monophasic (200J-360J) vs biphasic (200J-360J) AED. 2002-2004. N=168. Mismatch between AED and manual defibrillator by paramedics in 20 patients; these patients were excluded in evaluation of events related to >1 shock.
Response to first shock -
Termination of VF (3sec): monophasic N=75/91 (82%) and biphasic N=65/74 (88%)
Organized rhythm (not further defined): monophasic N=24/91 (26%) and biphasic N=24/91 (34%)
No comparison of biphasic waveform defibrillation at different starting energies.


LOE 5 (animal), poor, supportive. Prospective study of defibrillation threshold as defined by energy and peak current in a canine model. N=11.
Peak current defibrillation threshold constant across impedance and voltage changes. Defibrillation threshold as defined by energy increased with increasing impedance.

LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospective, randomized evaluation of biphasic (120J) compared to monophasic (200J) transthoracic defibrillation. N=184.
Successful termination of VF with first shock in 97/98 (99%) of patients receiving biphasic shock and 80/86 (93%, p=0.05) receiving monophasic


LOE 2, poor, supportive outcome E, neutral BC. IHCA, prospective, semi-randomized study of low (200 to 299J), intermediate (300-399J), or high energy (400-499J) for first shock in transthoracic defibrillation. Energy level of subsequent shocks determined by provider. Proportion of patients defibrillated after low dose (n=33, 39%) was lower than intermediate (n=36, 58%) and high dose (n=32, 56%).


LOE 4, good, neutral. OHCA, prospective randomized non-blinded (at EMS level) trial of monophasic escalating dose (200- 200 - 360J) compared to biphasic escalating dose (120-150-200J) defibrillation. N=538.
Improved termination of VF with biphasic compared to monophasic, underpowered for survival. Organized rhythm at 5sec after defibrillation was seen in 48/161 (29.8%) treated with biphasic waveform and 35/146 (24.0%) treated with monophasic waveform.
No comparison of biphasic waveform defibrillation at different starting energies.


LOE 5 (animal), poor, neutral. Prospective randomized non-blinded evaluation of monophasic (200-300-360J) compared to biphasic (150-150-150J) transthoracic defibrillation of a swine model of VF arrest. N=38. Duration of VF arrest 5 minutes. Successful termination of VF with first shock in 5/10 (50%).
No comparison of biphasic waveform defibrillation at different starting energies.


LOE 5 (animal), poor, neutral. Prospective, randomized, non-blinded evaluation of escalating monophasic or biphasic defibrillation (200J-300J-360J) on VF of 30 and 90s duration in a swine model. N=21.
Successful termination VF (30sec) with first shock was 60% (6/10) with monophasic and 64% (7/11) with biphasic.
No comparison of biphasic waveform defibrillation at different starting energies.


LOE 5 (animal), good, neutral. Prospective, randomized, non-blinded evaluation of escalating monophasic or biphasic defibrillation (200-300-360J) or fixed energy biphasic (150J) in a swine model. Duration of VF=5. N=68.
Comparable first shock success rate and equal proportions achieved ROSC.


VF terminated with first shock in 39/44 (89%) and 100% within 3 shocks.
No comparison of biphasic waveform defibrillation at different starting energies, thus considered case series for LOE.


LOE 5 (at time of ICD testing), good, opposing. Lab at time of ICD testing, prospectively randomized and blinded to two energy levels of truncated biphasic transthoracic (115J and 130J) and monophasic damped sine waveform (200J). N=28.
For each transthoracic pulse, the percent defibrillation efficacy was 97%. Less ECG evidence of myocardial dysfunction with lowest energy biphasic waveform.

LOE 5 (pediatric), fair, neutral. OHCA, retrospective cohort evaluating monophasic shock energy on survival. N=57. No association between shock dose and survival.


LOE 4, fair, neutral. OHCA, prospective randomized clinical trial of monophasic (both truncated exponential and damped sine) with traditional escalating dose to biphasic fixed dose defibrillation (150J). 1996-1998, four centers, N=246; analysis limited to those presenting in VF (N=115).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Biphasic</th>
<th>Monophasic</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination of VF (5sec) with first shock</td>
<td>44/48 (92%)</td>
<td>44/67 (66%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.


LOE 1, good, neutral. OHCA, prospective, randomized, blinded, clinical trial of a fixed lower-energy biphasic (150-150-150J) and an escalating higher-energy biphasic (200-300-360J) defibrillation protocol. 2002-2005, 3 sites. N=221.

<table>
<thead>
<tr>
<th>Electrical Outcomes on clustered on single or multiple Electrical Outcome</th>
<th>Fixed lower-energy</th>
<th>Escalating higher-energy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination VF (5sec)</td>
<td>99/114 (86.8%)</td>
<td>95/107 (88.8%)</td>
<td>0.81</td>
</tr>
<tr>
<td>First shock only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organized rhythm (60sec)</td>
<td>43/112 (38.4%)</td>
<td>36/98 (36.7%)</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Superior termination of VF and return of organized rhythm among patients requiring multiple shocks, no difference among patients requiring only one shock. No difference in ROSC, survival, or neurologic recovery. Benefit in electrical outcome appears related to escalating energy, not starting energy.


LOE 4, poor, neutral. OHCA, retrospective, cohort with historical controls to compare biphasic escalating dose (120-150-200J) transthoracic defibrillation to monophasic waveform of escalating dose (200-300-360J). 2000-2001. N=264. Successful termination of VF with 120J biphasic in 95/141 (67%, 95% CI: 59%–75%) and 116/141 (82%) within 3 shocks.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospective, randomized evaluation of escalating biphasic (150-200J) compared to escalating monophasic (150-360J) transthoracic defibrillation after failed internal shocks.

No comparison of higher to lower starting energy biphasic defibrillation.


LOE 5 (animal), good, neutral. Prospective randomized factorial design testing single shock vs 3-shock protocol and fixed dose biphasic (150J-150J-150J) vs escalating dose biphasic (200J-300J-360J) defibrillation in a pig model. N=44. No difference in first shock efficacy between 150J biphasic (10/20) and 200J biphasic (15/22) defibrillation.


Return of organized rhythm after first shock with biphasic defibrillation at 200J was 69% (35/51) and with monophasic at 200J was 45% (31/69).


LOE 5 (animal), poor, neutral. Prospective study of monophasic defibrillation compared to two waveforms of biphasic defibrillation to determine defibrillation thresholds for these waveforms in a dog model. Duration of VF 15 sec and 5 min.
Lower defibrillation thresholds observed for biphasic waveforms. The defibrillation thresholds remained statistically unchanged for longer duration VF treated with biphasic waveforms.


LOE 5 (animal), poor, supportive. Prospective study of biphasic defibrillation thresholds for electrically induced and spontaneous VF secondary to ischemia in dog and pig models.
Ischemia induced VF has higher defibrillation thresholds than electrically induced VF.


LOE 5 (animal), good, neutral. Prospective randomized comparison of different waveform and energy protocols in a swine model. Biphasic energy protocols were as follows: fixed low dose (150-150-150J), escalating high dose (200-300-360J), escalating low dose (120-150-200J) and escalating dose (“low”-“high”-“high”).
No difference in first shock efficacy noted for low impedance models. With higher impedance, higher starting dose was associated with greater first shock efficacy (62% for 150J, 92% for 200J, 82% for 120J, 64% for “low” energy).


LOE 2, fair, neutral. OHCA, prospective pseudo-randomized (site) non-blinded evaluation of fixed dose biphasic (150-150-150J) vs escalating dose biphasic (100-150-200J) defibrillation. 2002-2003, N=78 (40 fixed dose vs 38 escalating dose) with 224 episodes of VF (107 fixed dose vs 117 escalating dose). Analysis post-exclusion of energy violations (12 fixed dose and 39 escalating dose).

<table>
<thead>
<tr>
<th>Shock</th>
<th>Escalating dose (N=79)</th>
<th>Fixed dose (N=95)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46 (58%)</td>
<td>61 (64%)</td>
<td>“NS”</td>
</tr>
<tr>
<td>2</td>
<td>65 (82%)</td>
<td>74 (78%)</td>
<td>“NS”</td>
</tr>
<tr>
<td>3</td>
<td>73 (92%)</td>
<td>79 (83%)</td>
<td>0.029</td>
</tr>
</tbody>
</table>

No difference in first shock efficacy for starting energies of 100J compared to 150J. Termination of VF within 3 shocks seen with lower starting energy and escalating dose compared to higher starting energy fixed dose.


No difference in ROSC or survival to discharge among groups.


LOE 4, poor, neutral. OHCA, retrospective, cohort of fixed energy (150J) biphasic defibrillation. 1996-1997. N=10. First shock effectively terminated VF in 7/10 (70%) with termination of 42/51 (82%) total episodes of VF.
No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.


No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.


First shock efficacy 45/49 (92%, 95% CI 81-97%).
No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.

First shock efficacy 57/62 (92%, 95% CI 83-97%).
No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.


First shock efficacy 92/102 (90%, 95% CI 83-95%).
No comparison of higher to lower starting energy biphasic defibrillation, thus considered case series for LOE.


LOE 5 (animal), good, neutral outcome AB, opposed outcome E. Prospective randomized non-blinded evaluation of 3 levels of defibrillation energy (2, 10, or 20J) on post-defibrillation myocardial function. Duration of VF = 10 minutes. N=15
All animals had ROSC with single shock. Increased energy associated with decreased myocardial function post-shock.


LOE 5 (animal), poor, neutral. Prospective study of transthoracic defibrillation thresholds with monophasic or biphasic waveform in a swine model. Duration of VF=10 sec or 1 minute. N=12
Lower defibrillation thresholds with biphasic waveform. No difference in thresholds for within waveforms for different durations of VF arrest.


LOE 5 (animal), fair, supportive. Prospective evaluation of biphasic defibrillation success (termination of VF at 5sec) and weight in a pig model. N=22.
For low energy shocks, success of defibrillation was associated with weight, but all shocks higher energy shocks (>150J) terminated VF regardless of weight.


LOE 5 (animal), poor, supportive. Prospective randomized evaluation comparing biphasic and triphasic defibrillation pulses of very low energy (range 50-100-150J) in a pig model. N=14
Increasing shock efficacy with increasing energy. Shocks provided in random order, thus unclear impact of order of energy in series. Triphasic shocks more effective throughout energies tested.
Biphasic versus Monophasic Defibrillation Waveform


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospectively randomized non-blinded comparison of monophasic escalating (200-300-360J and fixed 360J) versus biphasic escalating (200-300J and fixed 300J) transthoracic defibrillation for termination of VF. N=118.
First shock successful in 100% of patients treated with biphasic and >96% success for both groups treated with monophasic.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospectively randomized and blinded to two energy levels of truncated biphasic transthoracic (115J and 130J) and monophasic damped sine waveform (200J). N=30.
For each transthoracic pulse, the percent defibrillation efficacy was 97%.


LOE 5 (at time of ICD), good, neutral. Lab at time of ICD, prospective, randomized, blinded study comparing first shock efficacy of monophasic (200J or 360J) compared to biphasic (115 or 130J) transthoracic defibrillation. N=294.
First shock effectively terminated VF with 115J biphasic in 86/97 (89%), with 130J biphasic in 144/167 (86%), with 200J monophasic in 143/166 (86%), and with 360J monophasic in 80/83 (96%). Differences in efficacy did not achieve statistical significance.


LOE 3, good, supportive outcome E, neutral outcomes ABC. OHCA, retrospective cohort, BTE (fixed and escalating) vs MDS vs MTE, N=366.
Grp 1: N=105, BTE 150-150-150J or BTE, 150-200-360J;
Termination VF [5sec] with 1 shock 89.5%, with < 3 shocks 97.1%; Conversion [60sec] with 1 shock 40%
ROSC 55.2%, Admitted 53.3%, Survival 20.0%;
Grp 2: N=193, MDS, 200-200-360J;
Termination VF with 1 shock 83.9%, with < 3 shocks 95.9; Conversion with 1 shock 25.4%
ROSC 65.3%, Admitted 56.6%, Survival 29.5%
Grp 3: N=68, MTE, 200-200-360J
Termination VF with 1 shock 63.2%, with < 3 shocks 85.3; Conversion with 1 shock 26.5%
ROSC 64.7%, Admitted 61.8%, Survival 39.7


LOE 5 (animal), poor, neutral. Prospective evaluation of monophasic and biphasic defibrillation waveforms ranging from 7 to 100J energy. Waveform and energy applied in random order to piglets of varying size to model infant and child. N=35
Termination of VF increased with increasing energy, with biphasic achieving >80% termination of VF by 20J in infant model and 30J in child model; monophasic required 50J in infant and 70J in child to achieve similar rates.


LOE 5 (animal), good, neutral. Prospective randomized evaluation of monophasic and biphasic shocks at five energy levels (70, 100, 200, 300, and 360J) in each animal, N=13. Duration of VF 15 seconds. Defibrillation success increased as energy increased for both waveforms. Biphasic shocks achieved higher success rates compared to monophasic shocks at 70J and 100J, but no difference in efficacy at higher energies.


LOE 5 (lab at time of ICD), good, supportive outcome E, neutral outcome A. Meta-analysis of randomized trials comparing monophasic and biphasic transthoracic defibrillation conducted in lab at time of ICD testing. 7 randomized trials identified, pooled analysis of same nominal energy N=398.
Compared to 200J monophasic shocks, 200J biphasic shocks reduced the risk of asystole or persistent VF after the first shock by 81% (RR=0.19, 95%CI: 0.06–0.60).

LOE3, good, supportive outcome E, neutral outcomes AC. OHCA, retrospective cohort, MTE vs BTE, 2000-2004 (MTE 2000-2002, BTE 2002-2004), N=485. More defibrillations required with monophasic defibrillation to achieve ROSC compared to BTE (3.5 vs 2.6, p=0.015). No difference observed in ROSC, survival to discharge, or discharge to home between MTE and BTE.


No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.


All VF episode defibrillation (at 5 sec) with ≤ 3 shocks:
Monophasic 179/210 (85%, 95% CI 79-90%) vs Biphasic 128/129 (99%, 95% CI 96-100%); p<0.0001
Mean shocks per patient episode:
Monophasic 2.4±2.5 vs Biphasic 1.20±0.2; p<0.07
No difference in ROSC or survival to hospital discharge.


LOE 5 (at time of ICD), good, supportive. Lab at time of ICD, prospective, randomized evaluation of monophasic (200J) vs biphasic (200J) transthoracic defibrillation. N=171.
Termination with first shock: biphasic defibrillation 81/93 (97.6%) vs monophasic 75/88(85.2%); p=0.005


LOE 5 (at time of ICD), good, supportive. Lab at time of ICD testing, randomized, prospective trial of monophasic (200J) compared to biphasic (130J or 200J) for transthoracic defibrillation. Duration of VF=19 seconds. N=115.
First shock effectively terminated VF: Monophasic 200J - 61/68 (87.9%, 95% CI 79.9-95.8%); Biphasic 130J – 39/47 (83%, 95% CI 69.2-92.4%); Biphasic 200J – 39/39 (100%, 95% CI 91-100%). No significant difference in post-shock hemodynamic quantities.


LOE 5 (at time of ICD or EP testing), poor, neutral. Lab at time of ICD or EP testing, evaluation of biphasic (150J) waveform for transthoracic defibrillation compared to an historic control. Duration of VF=16 seconds. N=96.
Biphasic 150J successfully terminated VF in 97.4% with first shock and successive fixed dose biphasic shocks effectively terminated VF in remaining two patients. In historical control period, monophasic 200J terminated VF in 61/68 (89.7%) and statistically equivalent to biphasic.


LOE 5 (animal), poor, supportive. Prospective study of defibrillation threshold with increasing duration of VF (5 to 30 sec) in an isolated rabbit heart model. Energy required for defibrillation with either waveform increased with duration of VF. Energy level required for defibrillation lower with biphasic pulse at all time points.


LOE 1, good, supportive. OHCA, prospective blinded randomized clinical trial of monophasic (200J ?) vs biphasic defibrillation (200J ?). Larger proportion in organized rhythm at 60 sec following biphasic (N=35, 69%) compared to following monophasic (N=31, 45%) RR=1.53 (95% CI 1.11-1.20).

LOE 1, good, neutral. OHCA, prospective randomized (at the level of EMS unit) clinical trial of monophasic (200-200-360J) vs biphasic (200-200-360J) AED. 2002-2004. N=168.
Mismatch between AED and manual defibrillator by paramedics in 20 patients; these patients were excluded in evaluation of events related to >1 shock.
Response to first shock -
Termination of VF (5sec): monophasic N=75 (82%) vs biphasic N=65 (88%) (P=0.33)
Organized rhythm: monophasic N=24 (26%) vs biphasic N=24 (34%) (P=0.30)
Sustained ROSC: monophasic N=18 (20%) vs biphasic N=18 (24%) (P=0.51)
Subsequent shocks –
Paralleled observations for the first shock
No statistically significant differences in survival –
Monophasic: Admitted alive to hospital N=58 (73%), discharged alive N=27 (34%), discharged home N=18 (23%)
Biphasic: Admitted alive to hospital N=52 (76%), discharged alive N=28 (41%), discharged home N=16 (24%)


Lower defibrillation thresholds with biphasic, successful defibrillation of prolonged VF that failed to terminate with monophasic shocks.


LOE 5 (at time of ICD), good, supportive. Lab at time of ICD, prospective, randomized evaluation of biphasic (120J) compared to monophasic (200J) transthoracic defibrillation. N=184.
First shock effective at terminating VF in 97/98 (99%) of patients receiving biphasic shock and 80/86 (93%, p=0.05) receiving monophasic.


LOE 1, fair, supportive outcome E, neutral ABCD. OHCA, prospective randomized non-blinded (at EMS level) trial of monophasic escalating dose (200-200-360J) compared to biphasic escalating dose (120-150-200J) defibrillation. N=538.
Improved termination of VF with biphasic compared to monophasic, underpowered for survival.

Outcomes after one to three shocks:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Biphasic</th>
<th>Monophasic</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organized rhythm (5 sec)</td>
<td>90/163 (55.2%)</td>
<td>66/149 (44.3%)</td>
<td>0.05</td>
</tr>
<tr>
<td>ROSC</td>
<td>61/164 (37.2%)</td>
<td>55/149 (36.9%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Survival to discharge</td>
<td>8/163 (4.9%)</td>
<td>6/147 (4.1%)</td>
<td>“NS”</td>
</tr>
</tbody>
</table>


LOE 5 (animal), good, neutral. Prospective randomized non-blinded evaluation of monophasic (200-300-360J) compared to biphasic (150-150-150J) transthoracic defibrillation of a swine model of VF arrest. N=38. Duration of VF arrest 5 minutes. Equivalent outcomes across treatment groups.


LOE 5(animal), good, neutral. Prospective, randomized, non-blinded evaluation of escalating monophasic or biphasic defibrillation (200-300-360J) on VF of 30 and 90s duration in a swine model. N=21.
No difference in outcomes (termination of VF or myocardial function post-shock) between groups.


LOE 5 (animal), good, neutral. Prospective, randomized, non-blinded evaluation of escalating monophasic or biphasic defibrillation (200-300-360J) or fixed energy biphasic (150J) in a swine model. Duration of VF=5. N=68.
Comparable first shock success rate and equal proportions achieved ROSC.

VF terminated with first shock in 39/44 (89%) and 100% within 3 shocks. No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.

LOE 5 (at time of ICD testing), good, supportive. Lab at time of ICD testing, prospectively randomized and blinded to two energy levels of truncated biphasic transthoracic (115J and 130J) and monophasic damped sine waveform (200J). N=28.
For each transthoracic pulse, the percent defibrillation efficacy was 97%. Less ECG evidence of myocardial dysfunction with biphasic compared to monophasic pulse

LOE 5 (animal), poor, supportive. Prospective, randomized, blinded study of transthoracic defibrillation with monophasic waveform compared to biphasic waveform in a swine model. Duration of VF=8 min. N=34.
ROSC: Biphasic waveform 7/17 (41%), monophasic waveform 1/17 (6%). p=0.04

LOE 1, fair, supportive outcomes ADE, neutral BC. OHCA, prospective randomized clinical trial of monophasic (both truncated exponential and damped sine) with traditional escalating dose to biphasic fixed dose defibrillation (150J). 1996-1998, four centers, N=246; analysis limited to those presenting in VF (N=115). Underpowered for survival.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Biphasic</th>
<th>Monophasic</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Termination of VF (5sec) within 3 shocks</td>
<td>46/48 (96%)</td>
<td>49/67 (73%)</td>
<td>0.002</td>
</tr>
<tr>
<td>ROSC</td>
<td>39/48 (81%)</td>
<td>35/67 (52%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Survival to Hospital Discharge</td>
<td>16/48 (33%)</td>
<td>18/67 (27%)</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Superior termination of VF and ROSC with biphasic. No difference in survival.

Successful termination of VF with 120J biphasic in 95/141 (67%, 95% CI: 59%–75%) and 116/141 (82%) within 3 shocks. Comparatively, monophasic terminated VF in 49% following first shock and 72% within 3 shocks.

LOE 5 (at time of ICD), good, supportive. Lab at time of ICD, prospective, randomized evaluation of escalating biphasic (150-200J) compared to escalating monophasic (150-360J) transthoracic defibrillation after failed internal shocks. Overall success with biphasic 93% compared to monophasic 64%.
No comparison of fixed dose to escalating dose biphasic defibrillation.

LOE 5 (animal), good, supportive outcome E, neutral outcomes AB. Prospective randomized trial of escalating dose monophasic (200-300-360J) vs fixed dose biphasic (150-150-150J) defibrillation of two different durations of VF (4 minute and 7 minute) in a pig model. N=20.
No difference in ROSC or survival, less myocardial dysfunction with biphasic.

LOE 5 (animal), good, supportive outcome E, neutral outcomes AB. Prospective randomized trial of escalating dose monophasic (200-300-360J) vs fixed dose biphasic (150-150-150J) defibrillation in a pig model. Duration VF 10 minutes. N=20.
No difference in ROSC or survival, less myocardial dysfunction with biphasic.

LOE 1, fair, supportive. OHCA, prospective randomized blinded trial of first shock success after monophasic or biphasic defibrillation. 2000-2002. N=120. Return of organized rhythm after first shock was higher with biphasic (35/51, 69%) than with monophasic (31/69, 45%) (RR 1.53, 95% CI 1.11-2.10). No formal evaluation of multiple shocks. No statistically significant difference in survival to hospital discharge (RR 0.73, 95% CI 0.31-1.70).


LOE 5 (animal), poor, neutral. Prospective study of monophasic defibrillation compared to two waveforms of biphasic defibrillation to determine defibrillation thresholds for these waveforms in a dog model. Duration of VF 15 sec and 5 min. Lower defibrillation thresholds observed for biphasic waveforms. The difference in defibrillation thresholds was larger with longer duration of VF as the thresholds remained statistically unchanged for biphasic waveforms, but increased for monophasic waveforms.


LOE 5 (animal), good, supportive. Prospective randomized comparison of different waveform and energy protocols in a swine model. Biphasic energy protocols were as follows: fixed low dose (150J-150J-150J), escalating high dose (200J-300J-360J), escalating low dose (120J-150J-200J) and escalating dose (“low”- “high”- “high”). No difference in shock efficacy noted for low impedance. With higher impedance, escalating high dose more effective at terminating VF within 3 shocks (OR 3.6, 95% CI 2.3-5.4 when compared to next best of “low”- “high”- “high” whose delivered energy was 184J in the low setting).


<table>
<thead>
<tr>
<th>Shock</th>
<th>Escalating dose (N=79)</th>
<th>Fixed dose (N=95)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46 (58%)</td>
<td>61 (64%)</td>
<td>“NS”</td>
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<tr>
<td>2</td>
<td>65 (82%)</td>
<td>74 (78%)</td>
<td>“NS”</td>
</tr>
<tr>
<td>3</td>
<td>73 (92%)</td>
<td>79 (83%)</td>
<td>0.029</td>
</tr>
</tbody>
</table>

No comparison of biphasic to monophasic defibrillation, thus considered case-series for LOE.


LOE 4, poor, neutral. OHCA, retrospective, cohort of fixed energy (150J) biphasic defibrillation. 1996-1997. N=10. First shock effectively terminated VF in 7/10 (70%) with termination of 42/51 (82%) total episodes of VF. No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.


LOE 4, poor, neutral. OHCA, retrospective, cohort of patients treated for OHCA due to VF with fixed-dose (150-150-150J) biphasic defibrillators. 1996-2000. N=42 but results limited to 35 with witnessed arrest. Survival reported as comparable to that observed in previous studies with escalating higher dose monophasic defibrillation; comparison group not defined. No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.


LOE 4, fair, neutral. OHCA, retrospective cohort evaluating incidence of refibrillation and outcome in management of VF OHCA treated with fixed dose (150-150-150J) biphasic defibrillation. 1996-2001. N=49. Although refibrillation occurred frequently (61%), it was not associated with ROSC, survival to discharge, or neurologically intact survival. No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.

LOE 4, fair, neutral. OHCA, retrospective, cohort evaluating association between successful defibrillation with fixed-dose (150-150-150J) biphasic defibrillator and patient weight. 1996-2002. N=62. No association observed between patient weight and successful defibrillation (defined as 5 sec post-shock rhythm non-shockable). No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.


LOE 4, fair, neutral. OHCA, retrospective, cohort evaluating transthoracic impedance on successful defibrillation with fixed-dose (150-150-150J) biphasic defibrillator. 1996-2001. N=102. No association between transthoracic impedance and successful defibrillation (defined as non-shockable rhythm at 5 sec). No comparison of biphasic to monophasic defibrillation, thus considered case series for LOE.


LOE 5 (animal), poor, supportive. Prospective study of transthoracic defibrillation thresholds with monophasic or biphasic waveform in a swine model. Duration of VF=10 sec or 1 minute. N=12 Lower defibrillation thresholds with biphasic waveform.


LOE 5 (animal), good, supportive. Prospective randomized non-blinded pig model evaluation of monophasic versus biphasic shocks on normal hearts and hearts with halothane induced LV dysfunction. Biphasic superior to monophasic in termination of VF at 5 sec.
Multiphasic versus Biphasic Defibrillation Waveform


LOE 5 (animal), poor, neutral. Determination of defibrillation thresholds for a range of triphasic and biphasic waveforms of varying tilts and phase-duration ratios as measured by a transvenous lead system in a pig model. Duration of VF = ?. N=16. Challenging to interpret study protocol and results. Minimal decrease in defibrillation threshold with some 80% tilt triphasic waveforms from 300-microF capacitor compared to similar biphasic waveforms.


LOE 5 (cell culture), fair, supportive. Determination of energy level for pacing threshold and arrhythmia threshold (defined as energy level resulting in 4 second arrest) with monophasic, biphasic, and triphasic waveforms in a myocardial cell culture model. N=9 per waveform.
Pacing threshold: Biphasic 0.672±0.007 V/cm; Triphasic 0.672±0.005 V/cm (p="ns")
Arrhythmia threshold: Biphasic 80.6 ± 1.3%; Triphasic 87.1 ± 0.7%
Safety factor (ratio of arrhythmia threshold to pacing threshold): biphasic 120.3; triphasic 130
Suggests triphasic waveform may result in defibrillation at similar threshold as biphasic, but have greater margin of safety to energy level that results in shock induced dysfunction.


LOE 5 (animal), fair, neutral. Non-randomized and randomized experiments to determine transthoracic defibrillation thresholds using conventional and rounded biphasic or triphasic waveforms in a pig model. Duration of VF = 10 sec. N=7 in randomized study.
Non-randomized studies:
A. Conventional biphasic truncated exponential vs rounded biphasic truncated exponential waveform – waveform rounding reduced defibrillation threshold by >15% for all durations of biphasic wave pulse (p<0.05 for all comparisons to conventional waveform).
B. Rounded biphasic truncated exponential vs Lown waveform – lower defibrillation threshold with rounded biphasic compared to Lown waveform (27%, p<0.05)
Randomized study: Comparison of 5 different rounded triphasic waveforms with total duration of 6 or 12ms and varying pulse ratios to 2 rounded biphasic waveforms (6 or 12ms with 1:1 pulse ratio) – no difference in defibrillation threshold between rounded biphasic and rounded triphasic waveforms.


LOE 5 (animal), fair, supportive. Defibrillation efficacy of Edmark monophasic, biphasic truncated exponential, and quadriphasic truncated exponential waveforms via transthoracic defibrillation in a dog model. Supplemental non-randomized study to determine defibrillation threshold for biphasic compared to triphasic waveforms. Duration of VF = 10 sec. N=15 with total of 810 fibrillation-defibrillation episodes.

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</thead>
<tbody>
<tr>
<td>Edmark</td>
<td>31</td>
<td>9</td>
<td>27</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>Biphasic</td>
<td>47</td>
<td>51</td>
<td>69</td>
<td>42</td>
<td>49</td>
</tr>
<tr>
<td>Quadruphasic</td>
<td>51</td>
<td>53</td>
<td>78</td>
<td>49</td>
<td>71</td>
</tr>
</tbody>
</table>

Biphasic and Quadruphasic more successful than Edmark across all treatments (p<0.0001). Quadruphasic more successful than Biphasic at 138Ω-24J (p=0.01)
In defibrillation threshold testing, quadriphasic threshold (7.9A) was lower than biphasic threshold (8.9A, p=0.005)


LOE 5 (animal), fair, neutral. Defibrillation efficacy of transthoracic damped sinusoidal monophasic, biphasic truncated exponential, and overlapping encircling multipulse waveforms in a dog and swine model. Duration VF = 30 seconds. N=21 (dog) and 11 (swine).
Overlapping multipulse shock successfully defibrillated VF in >80% at energies of 50-99J compared to approximately 50% for biphasic and approximately 20% for damped sinusoidal. There was no difference in defibrillation efficacy between overlapping multipulse and biphasic when energy increased to >100J.

LOE 5 (animal), fair, supportive. Defibrillation efficacy (termination of VF at 5 sec) of transthoracic biphasic truncated exponential waveform compared to triphasic truncated exponential waveform in a pig model. Duration VF=30sec. N=49.

I. Comparison of equal-duration pulses:
   a. Biphasic 7.2/7.2ms compared to triphasic 4.8/4.8/4.8ms:
      Greater defibrillation efficacy with triphasic at energies <90J (p<0.05)
   b. Biphasic 5/5ms compared to triphasic 5/5/5ms:
      Greater defibrillation efficacy with triphasic at energies 40-65J (p<0.05)

II. Comparison of equal-energy pulses:
   a. Biphasic 3.3/11.1 ms compared to triphasic 2.0/3.2/9.2ms:
      Greater defibrillation efficacy with triphasic across all energies (p<0.05)

III. Combined comparison of post-shock myocardial dysfunction

<table>
<thead>
<tr>
<th></th>
<th>Biphasic Waveform (estimated probability)</th>
<th>Triphasic Waveform (estimated probability)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-shock VT</td>
<td>0.23</td>
<td>0.09</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Post-shock asystole</td>
<td>0.17</td>
<td>0.07</td>
<td>0.03</td>
</tr>
<tr>
<td>Post-shock ST-segment elevation</td>
<td>0.08</td>
<td>0.04</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Suggests triphasic waveforms of equal pulse duration result in termination of VF at lower energies and are associated with less post-shock myocardial dysfunction.


LOE 5 (animal), fair, supportive. Semi-randomized study of defibrillation efficacy (termination of VF at 5 sec) with biphasic truncated exponential and triphasic truncated exponential defibrillation waveforms in an open-chest swine model. Duration of VF=30sec. N=22 with four shocks at each energy level. Over range of energies tested (3J -30J) defibrillation efficacy with triphasic waveform (range 44-86%) better than biphasic waveform (range 20-70%; p<0.01). No statistically significant differences in post-shock arrhythmias or hemodynamics.


LOE 5 (animal), fair, supportive. Semi-randomized study of defibrillation efficacy (termination of VF at 5sec) with triphasic truncated exponential and quadriphasic truncated exponential defibrillation waveforms in a swine model. Duration of VF=30 sec. N=16. Quadriphasic superior to triphasic in high-transthoracic impedance model at >65J (OR 4.17: 95% CI 1.65-10.58; p=0.02) No difference between defibrillation efficacy at lower energies or in low-impedence model. No difference in post-shock arrhythmias.
One Shock versus Three Stacked Shocks Protocol


LOE 3, good, supportive outcomes CD, neutral outcomes AB. OHCA, before and after comparison of 2000 AHA/ILCOR guidelines for OHCA (which included recommendation for up to 3 shocks for persistent VF) to minimally interrupted cardiac resuscitation (MICR) (which included one shock when indicated). Analysis also included a protocol compliance analysis, but this did not evaluate one vs three shocks. 2005-2007. N= 886.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Before MICR (%)</th>
<th>After MICR (%)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to discharge</td>
<td>4/218 (1.8)</td>
<td>36/668 (5.4)</td>
<td>3.0 (1.1-8.9)</td>
</tr>
<tr>
<td>Survival of witnessed VF</td>
<td>2/43 (4.7)</td>
<td>22/131 (17.6)</td>
<td>8.6 (1.8-42.0)</td>
</tr>
<tr>
<td>ROSC</td>
<td>34/218 (15.6)</td>
<td>154/668 (23.1)</td>
<td>1.3 (0.8-2.0)</td>
</tr>
<tr>
<td>Survival to admission</td>
<td>35/218 (16.1)</td>
<td>113/668 (16.9)</td>
<td>0.8 (0.5-1.2)</td>
</tr>
</tbody>
</table>

Unclear how much of observed effect size is related to protocol changes for CPR and ventilation as opposed to single shock protocol.


LOE 5 (animal), fair, neutral. Study determined the ability of each transthoracic shock in a stacked shock sequence to return spontaneous circulation in a pig model. Duration VF = 8 min. N=60.

Results reported as ROSC after each shock, but failed to account for changing number of animals at risk due to successful defibrillation.

Corrected for animals at risk for each shock:

<table>
<thead>
<tr>
<th>Shock</th>
<th>ROSC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48/60 (80)</td>
</tr>
<tr>
<td>2</td>
<td>9/12 (75)</td>
</tr>
<tr>
<td>3</td>
<td>3/3 (100)</td>
</tr>
</tbody>
</table>

When animals at risk of failed shock are considered as opposed to all animals, there was no apparent difference in shock efficacy with each sequential shock in a stacked shock protocol.
No comparison of single shock to stacked shock protocol.


LOE 2, poor, supportive. OHCA, retrospective, non-blinded, probability of ROSC by ECG signal characteristics as a function of hands-off interval before defibrillation shock. Higher probability or ROSC with shorter hands-off interval. Applicability limited by lack of data as to hands-off interval in relation to single shock or stacked shocks. Additionally, true ROSC would have been a preferred outcome measure as opposed to probability of ROSC by ECG characteristics.


LOE 3, good, supportive. OHCA, before and after comparison of AHA/ILCOR 2000 guideline directed care to revised protocol with single shock without rhythm reanalysis or postdefibrillation pulse check and 2 minutes of post shock CPR for out-of-hospital VF. 2002-2006. N=509.

<table>
<thead>
<tr>
<th>Outcome, % (N)</th>
<th>Control Period (N=374)</th>
<th>Intervention Period (N=134)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival to Hospital</td>
<td>59.6 (223)</td>
<td>73.9 (99)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Survival to Discharge</td>
<td>32.8 (123)</td>
<td>45.5 (61)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Discharge to Home</td>
<td>25.6 (96)</td>
<td>36.6 (49)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Unclear how much of observed effect size is related to protocol changes for post shock CPR as opposed to single shock protocol.


LOE 5 (animal), fair, supportive. Evaluation of ROSC following defibrillation with either 40 second duration of hands-off interval prior to shock or continuous CPR (also no CPR arm – not relevant to question). Duration VF = 6.5 min. N=12.

ROSC: 40 second hands off 1/6 (17%) compared to continuous CPR 5/6 (83%)

LOE 5 (animal), good, supportive. Prospective, randomized, non-blinded, factorial design to test one versus three stacked shock protocols among defibrillators with a short hands-off time and longer hands-off time. Duration of VF = 7 minutes. N=44.

Outcomes by AED and shock protocol:

<table>
<thead>
<tr>
<th>Outcome, N (95% CI)</th>
<th>Short hands-off One shock</th>
<th>Short hands-off Three shocks</th>
<th>Longer hands-off One shock</th>
<th>Longer-hands off Three shocks</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROSC</td>
<td>11/11 (76-100%)</td>
<td>10/11 (64-100%)</td>
<td>11/11 (76-100%)</td>
<td>4/11 (14-65%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>72 hr survival</td>
<td>11/11 (76-100%)</td>
<td>10/11 (64-100%)</td>
<td>11/11 (76-100%)</td>
<td>4/11 (14-65%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Post-shock ST-segment depression, mV</td>
<td>0.09 (0.04-0.22)</td>
<td>0.25 (0.21-0.29)</td>
<td>0.33 (0.20-0.41)</td>
<td>0.31 (0.21-0.42)</td>
<td>&lt;0.007</td>
</tr>
</tbody>
</table>

Outcome most affected by hands-off delay. Suggestion of decreased post-shock myocardial dysfunction with one-shock protocol as measured by ECG changes. Small favorable changes also noted for post-shock LV ejection fraction as compared to baseline with one shock compared to three.