

WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care**Worksheet author(s)**

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Date Submitted for review: 25 February 2010**Clinical question.**

In adult cardiac arrest (prehospital [OHCA], in-hospital [IHCA]) (P), does the use of an escalating defibrillation protocol (I), when compared to a fixed energy protocol (C) increase outcome (e.g. return of spontaneous circulation) (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: Revision

Search strategy (including electronic databases searched).

PubMed (“heart arrest” OR “cardiopulmonary resuscitation” as MESH (headings)) AND (“electric countershock/therapy OR “electric countershock/methods” OR “electric countershock/standards” as MESH (headings)) OR (“resuscitation” as text word (all fields) AND “defibrillat* energy” as text words (all fields)) OR (“electric countershock” AND “clinical protocols” as MESH (headings))

EMBASE search using text words (all fields) “resuscitation” AND “defibrillat*” AND “energy”

Cochrane Library search using text words (all fields) (including Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials) (“heart arrest” OR “cardiopulmonary resuscitation”) AND (“electric countershock” OR “defibrillators”)

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 an energy protocol for defibrillation was evaluated. 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 624 (5 Feb 2010), EMBASE 164 (29 Sept 2009), Cochrane Library 240 (29 Sept 2009), AHA EndNote Master library 257 (10 Sept 2008).

A total of 115 studies met criteria for further review which resulted in identification of 69 studies pertinent to the clinical question. Of these, 1 study was LOE 1 (RCT), 3 studies were LOE 2 (non-randomised, concurrent controls), 22 LOE 4 (no controls), and 43 LOE 5 (not directly related or animal studies).

Articles Identified for Further Review	116	
Articles Included in Full Review		70
Human Articles		40
Animal Articles		29

Summary of evidence Evidence Supporting Clinical Question

Good	Stiell 2007, E ¹			Heavens 1998, BCE ⁷ Koster 2008, E	<i>Berg 2005, E²</i> <i>Clark 2002, E⁸</i> <i>Higgins 2000, E¹⁰</i> <i>Niemann 2004, E¹</i> <i>Tang 2006, AE⁶</i> <i>Walker, 2003 E¹</i>
Fair		Walsh 2004, E ¹			
Poor				Morgan, 1984 E ⁹	<i>Bardy 1988, E⁷</i> <i>Clark 2001, E⁸</i> <i>Geddes 1974, E⁹</i> <i>Jones 1990, E⁸</i> <i>Lerman 1987, E⁹</i> <i>Walcott 2002, E⁵</i> <i>Zelinka 2007, E⁸</i> <i>Zhang 2003, E⁴</i>
	1	2	3	4	5
Level of evidence					

- 1 – Biphasic escalating vs Biphasic fixed
- 2 – Biphasic escalating (high dose) vs biphasic escalating (low dose)
- 3 – Biphasic escalating vs monophasic escalating
- 4 – Biphasic escalating vs triphasic escalating
- 5 – Biphasic escalating
- 6 – High energy biphasic escalating vs low energy biphasic fixed (one shock protocol)
- 7 – Monophasic escalating
- 8 – Biphasic and monophasic energy evaluation
- 9 – Monophasic energy evaluation
- 10 – Biphasic vs monophasic (first shock efficacy)

A = Return of spontaneous circulation
B = Survival of event

C = Survival to hospital discharge
D = Intact neurological survival

E = Other endpoint
Italics = Animal studies

Evidence Neutral to Clinical question

Good	Stiell 2007, ABCD ¹			Carpenter 2003, ABCE ¹⁵ Freeman 2008, ACE ⁵ Hess 2004, ABCE ^{†11} Hess 2008, ADE ^{†11} Koster 2006, E ⁵ Kudenchuk 2006, ABCDE ⁵ Morrison 2005, ABCD ⁵ van Alem 2003, E ⁹ Walker 2009, E ¹	<i>Bain 2001, E³</i> <i>Bardy 1995, E^{†9}</i> <i>Bardy 1996, E^{†9}</i> <i>Berg 2005, ABE²</i> <i>Greene 1995, E⁹</i> <i>Leng 2000, ABE⁵</i> <i>Mittal 1999, E⁹</i> <i>Niemann 2000a, AE¹⁰</i> <i>Niemann 2000b, E⁵</i> <i>Niemann 2003a, AE⁴</i> <i>Reddy 1997, E^{†9}</i> <i>Tang 1999, ABE¹⁰</i> <i>Tang 2001, ABE¹⁰</i> <i>Tang 2004, AE¹¹</i> <i>Tang 2006, AE⁸</i> <i>Xie 1997, ABE¹⁴</i> <i>Yamaguchi 2002, E¹⁴</i>
Fair				Gliner 1998, AE ^{§11} Gliner 1999, AC ¹⁰ Schneider 2000, BCD ¹⁰ White 2002, ABCDE ^{§11} White 2004, ABCE ^{§11}	<i>Berg 2005, E⁷</i> <i>Rossano 2006, C¹⁴</i> <i>Szili-Torok 2002, E⁵</i> <i>Zhang 2001, E⁹</i> <i>Zhang 2002, E⁷</i>

				White 2005, ABCE ^{§11}	
Poor		Jakobsson 1989, BE ¹²		Morgan 1984, BC ¹⁴ Poole 1997, E ^{§11} Stohtert 2004, E ⁵ White 1997, E ^{§11} White 2001, ABCE ^{§11}	Higgins 2004, E ¹¹ <i>Killingsworth 2002, E⁷</i> <i>Niemann 2003b, E⁵</i> <i>Scheatzle 1999, A⁵</i> <i>Tang 2002, AE¹¹</i> <i>Walcott 1998, A⁷</i> <i>Yamanouchi 1999, E¹⁶</i>
	1	2	3	4	5
Level of evidence					

* Overlapping patients

† Overlapping patients

‡ Overlapping patients

§ Overlapping patients

1 – Biphasic escalating vs biphasic fixed

2 – Biphasic escalating (high dose) vs biphasic escalating (low dose)

3 – Biphasic (fixed and escalating) vs monophasic (fixed and escalating)

4 – Biphasic escalating vs biphasic fixed vs monophasic escalating

5 – Biphasic escalating vs monophasic escalating

6 – Biphasic escalating

7 – Biphasic energy evaluation

8 – High energy biphasic escalating vs low energy biphasic fixed (one shock protocol)

9 – Biphasic vs monophasic (first shock success)

10 – Biphasic fixed vs monophasic escalating

11 – Biphasic fixed

12 – Escalating monophasic vs fixed monophasic

13 – Monophasic escalating (high dose) vs monophasic escalating (high dose)

14 – Monophasic energy evaluation

15 – Biphasic (fixed and escalating) vs monophasic escalating

16 – Biphasic and monophasic energy evaluation

A = Return of spontaneous circulation

B = Survival of event

C = Survival to hospital discharge

D = Intact neurological survival

E = Other endpoint

Italics = Animal studies

Evidence Opposing Clinical Question

Good					
Fair				Gliner 1999, E ³ Schneider 2000, AE ³	
Poor		Jakobsson 1989, C ¹ Gascho 1979, BCE ²			
	1	2	3	4	5
Level of evidence					

1 – Escalating monophasic vs fixed monophasic

2 – Monophasic (first shock efficacy)

3 – Biphasic fixed vs monophasic escalating

A = Return of spontaneous circulation

C = Survival to hospital discharge

E = Other endpoint

B = Survival of event

D = Intact neurological survival

Italics = Animal studies

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

DISCUSSION: The advent of biphasic waveform external defibrillators lead to clinical trials comparing fixed low-energy impedance compensating biphasic external defibrillators to traditional monophasic defibrillators. Randomized and observational trials demonstrated fixed low-energy biphasic defibrillators terminated ventricular fibrillation more effectively than escalating dose monophasic defibrillators. However, it remained unclear if fixed energy biphasic defibrillation would remain superior when compared to escalating energy protocol biphasic defibrillation. The clinical question of this worksheet aims to determine whether an escalating defibrillation protocol increases survival and/or return of spontaneous circulation, given concerns about potential myocardial damage induced by higher energy shocks.

- The first clinical comparison of different biphasic energy levels and dosing regimens was conducted by Walsh et al. (Walsh 2004, 378). 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 with one study site using fixed energy (150-150-150J) biphasic protocol while the other site used escalating energy (100-150-200J) biphasic protocol. Among patients requiring 3 shocks for termination of ventricular fibrillation, a greater proportion successful defibrillation (defined in this study as discontinuation of ventricular fibrillation for >5 seconds) when receiving escalating dose protocol. No difference in successful defibrillation was seen for the first or second shocks. 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.

- An important clinical study was performed by Stiell et al. (Stiell 2007, 1511). This was a randomized controlled trial of 221 patients with out-of-hospital cardiac arrest due to ventricular fibrillation. The study demonstrated higher dose escalating energy protocol (200, 300, 360J) biphasic defibrillation was superior to fixed dose low energy (150-150-150J) biphasic defibrillation in converting ventricular fibrillation to an organized rhythm among patients requiring multiple shocks. However, neither return of spontaneous circulation or survival to hospital discharge were improved by higher energy escalating dose biphasic defibrillation.

- An observational analysis by Hess et al. (Hess 2008, 28) of fixed low-energy biphasic defibrillation for out-of-hospital cardiac arrest due to ventricular fibrillation suggested no loss in defibrillation efficacy with successive shocks for recurrent ventricular fibrillation. The proportion of patients with successful defibrillation, defined as termination of ventricular fibrillation for > 5 seconds, was relatively constant for successive shocks. Although the statistical analysis was robust including multiple regression analysis with generalized estimating equations to account for interrelatedness of shocks within each patient, an assessment of the statistical trend of successful defibrillation with successive shocks was not provided. Limitations include the

observational design and lack of a comparison group. Compared to the trial by Stiell et al., a higher proportion of patients were successfully defibrillated after first shock. This may represent a population more amenable to defibrillation and less likely to require higher defibrillation energies. Additionally, endpoints of interest differed between the two studies. The primary endpoint reported by Hess et al. was termination of ventricular fibrillation at 5 seconds after shock while the primary endpoint reported by Stiell et al. was the proportion of patients with organized rhythm 60 seconds after defibrillation.

- Of the large number of animal trials, only Walker et al. (Walker 2003, 73) and Niemann et al (Niemann 2004, 619) compared biphasic defibrillation of fixed dose and varying escalating dose protocols. In the study by Niemann et al., a higher proportion of swine were defibrillated with an escalating energy (15/18, 83%, 95% CI 59-96%) compared to a fixed dose protocol (5/17, 29%, 95% CI 10-56%). Additionally, nine of the 17 swine that could not be defibrillated within 3 shocks by a fixed energy biphasic waveform were successfully defibrillated with an escalating energy. The study by Walker et al. suggested escalating-dose biphasic defibrillation was more effective than fixed-dose energy in high transthoracic impedance models.
- The only human study of escalating monophasic compared to fixed monophasic defibrillation was conducted by Jacobsson et al. (Jacobsson 1989, 551). This was a retrospective study of OHCA treated with fixed high or low energy monophasic defibrillation and escalating monophasic defibrillation. A higher proportion of patients treated with fixed monophasic defibrillation at a high energy survived to discharge (n=11, 7%) compared to fixed low energy (n=3, 2%) or escalating monophasic defibrillation (n=2, 4%). No adjustment was undertaken for possible confounders in this retrospective analysis.

There is fair evidence supporting an escalating energy defibrillation algorithm in patients who fail to convert to an organized rhythm after first shock. Although no benefit in return of spontaneous circulation or survival to hospital discharge has been reported among patients receiving escalating dose defibrillation, a larger percentage convert to an organized rhythm suggesting a potential for improved survival. The lack of difference in conversion of ventricular fibrillation after first shock in the lower versus higher starting energies in the study by Stiell et al. suggests it is appropriate to start at a lower-energy to minimize potential post-defibrillation cardiac dysfunction.

Statistical summary of critical studies: Stiell 2007, 1511; Walsh 2004, 378; Hess 2008, 28

Summary of Stiell 2007, 1511:

- 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 was achieved after first shock in 99/114 (86.8%) treated with lower-energy and 95/107 (88.8%) treated with higher-energy (p=0.81). Similar outcomes were seen for organized rhythm (defined as at least two consecutive QRS complexes separated by no more than 5 seconds) within 60 seconds after first shock, with the endpoint achieved in 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).
- No evidence of significantly improved return of spontaneous circulation (fixed-lower energy 58/114 (50.9%) vs higher-energy biphasic 52/107 (48.6%), survival to 24 hours after arrest (fixed-lower energy 37/114 (32.5%) vs higher-energy biphasic 38/107 (35.5%), or survival to hospital discharge (fixed-lower energy 19/114 (16.7%) vs higher-energy biphasic 17/107 (15.9%).
- Despite randomization, the small sample size resulted in some unbalanced patient characteristics among treatment groups (most notably, initial rhythm of asystole in 6 patients treated with fixed dose compared to 0 patients treated with escalating dose). Analysis incorporating adjustment on baseline covariates was not conducted.

Summary of Walsh 2004, 378:

- Multicenter observational evaluation of fixed dose biphasic (150J-150J-150J) vs escalating dose biphasic (100J-150J-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).
- 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).

Summary of Hess 2008, 28:

- Retrospective cohort of patients treated with fixed low-dose biphasic AED. 1996-2007, N=103. No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.
- Termination of VF (≥ 5 seconds) was observed in 93/101 (92%) after first shock with recurrence or persistence of ventricular fibrillation in 63 patients. The proportion of patients whose VF was terminated after each shock remained relatively unchanged (success after second shock 58/63 (92.1%), after third shock 37/41 (90.2%), after fourth shock 18/21 (85.7%), after five or more shocks 27/31 (87.1%)).

- Although a statistical analysis of successive pairs of shocks (i.e. 1 vs 2, 2 vs 3, etc) demonstrated no difference in successful defibrillation, there was no assessment of trend.
- Refibrillation was not associated with a decrement in neurologically intact survival (OR 1.07, 95% CI 0.39-2.93, p=0.90).

REVIEWER'S CONFLICTS OF INTEREST:

Steven M. Bradley – Internist/Cardiology Fellow. No intellectual or commercial conflicts. Fellowship supported by VA HSR&D Post-MD Fellowship

Acknowledgements:

Graham Nichol for his mentorship in preparation of this worksheet.

Citation List

Bain, A. C., C. D. Swerdlow, et al. (2001). "Multicenter study of principles-based waveforms for external defibrillation." *Ann Emerg Med* 37(1): 5-12.

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 (200J-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, thus unable to compare effect of escalating vs fixed dose energy.

Bardy, G. H., T. D. Ivey, et al. (1988). "Prospective evaluation of initially ineffective defibrillation pulses on subsequent defibrillation success during ventricular fibrillation in survivors of cardiac arrest." *American Journal of Cardiology* 62(10 PART I): 718-722.

LOE 5 (at time of ICD), poor, supportive. Lab at time of ICD, prospective evaluation of energy required for defibrillation after failed defibrillation attempt. N=14.

Higher energy defibrillation shocks were required for rescue defibrillation after failed defibrillation attempts.

Bardy, G. H., B. E. Gliner, et al. (1995). "Truncated biphasic pulses for transthoracic defibrillation." *Circulation* 91(6): 1768-1774.

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%.

No comparison of fixed dose to escalating dose biphasic defibrillation.

Bardy, G. H., F. E. Marchlinski, et al. (1996). "Multicenter comparison of truncated biphasic shocks and standard damped sine wave monophasic shocks for transthoracic ventricular defibrillation. Transthoracic Investigators." *Circulation* 94(10): 2507-14.

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.

No comparison of fixed dose to escalating dose biphasic defibrillation.

Berg, M. D., R. A. Samson, et al. (2005). "Pediatric defibrillation doses often fail to terminate prolonged out-of-hospital ventricular fibrillation in children." *Resuscitation* 67(1): 63-7.

LOE 5 (pediatric), fair, neutral. OHCA, retrospective cohort, N=11. Pediatric dose shocks failed to terminate VF in 50% of children with OHCA due to VF.

Berg, R. A., R. A. Samson, et al. (2005). "Better outcome after pediatric defibrillation dosage than adult dosage in a swine model of pediatric ventricular fibrillation." *Journal of the American College of Cardiology* 45(5): 786-789.

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 with 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.

Carpenter, J., T. D. Rea, et al. (2003). "Defibrillation waveform and post-shock rhythm in out-of-hospital ventricular fibrillation cardiac arrest." *Resuscitation* 59(2): 189-96.

LOE 4, good, supportive. 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%

Grp3: 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

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Clark, C. B., Y. Zhang, et al. (2001). "Pediatric transthoracic defibrillation: Biphasic versus monophasic waveforms in an experimental model." Resuscitation 51(2): 159-163.

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.

Clark, C. B., Y. Zhang, et al. (2002). "Transthoracic biphasic waveform defibrillation at very high and very low energies: a comparison with monophasic waveforms in an animal model of ventricular fibrillation." Resuscitation 54(2): 183-6.

LOE 5 (animal), good, supportive. 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.

Freeman, K., G. W. Hendey, et al. (2008). "Biphasic defibrillation does not improve outcomes compared to monophasic defibrillation in out-of-hospital cardiac arrest." Prehosp Emerg Care 12(2): 152-6.

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. No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Gascho, J. A., R. S. Crampton, et al. (1979). "Determinants of ventricular defibrillation in adults." Circulation 60(2): 231-40.

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.

Geddes, L. A., W. A. Tacker, et al. (1974). "Electrical dose for ventricular defibrillation of large and small animals using precordial electrodes." J Clin Invest 53(1): 310-9.

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

Gliner, B. E., D. B. Jorgenson, et al. (1998). "Treatment of out-of-hospital cardiac arrest with a low-energy impedance-compensating biphasic waveform automatic external defibrillator. The LIFE Investigators." Biomed Instrum Technol 32(6): 631-44.

LOE 4, fair, neutral. OHCA, retrospective, cohort. Biphasic fixed energy (150J) defibrillation. 1996-1998. N=100 Successful termination of VF with 1st shock 86%, within 3 shocks 97%, ROSC 58%. No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Gliner, B. E. and R. D. White (1999). "Electrocardiographic evaluation of defibrillation shocks delivered to out-of-hospital sudden cardiac arrest patients." Resuscitation 41(2): 133-144.

LOE 4, fair, neutral. OHCA, retrospective cohort with historical controls, monophasic escalating dose (200-300-360J) AED (1990-1997, N=87) vs biphasic fixed dose (150J) AED (1996-1998, N=29).

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.

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Greene, H. L., J. P. DiMarco, et al. (1995). "Comparison of monophasic and biphasic defibrillating pulse waveforms for transthoracic cardioversion. Biphasic Waveform Defibrillation Investigators." Am J Cardiol 75(16): 1135-9.

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.

Termination with first shock: biphasic defibrillation 81/93 (97.6%) vs monophasic 75/88(85.2%); p=0.005

No comparison of fixed dose to escalating dose defibrillation.

Heavens, J. P., M. J. Cleland, et al. (1998). "Effects of transthoracic impedance and peak current flow on defibrillation success in a prehospital setting." *Ann Emerg Med* 32(2): 191-9.

LOE 4, good, supportive. 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 defibrillation and transthoracic impedance by shock number:

Shock number	Defibrillation Success(5 sec)	TTI (Omega, mean±SD)
1	79/310 (25.5)	84.5 (22.9)
2	45/187 (24.1)	89.0 (25.5)
3	25/111 (22.5)	90.1 (25.4)

Despite increasing TTI, defibrillation success remained fairly constant with escalating energy.

Monophasic AED; no comparison to alternate dosing and/or biphasic waveform, thus considered case series for LOE.

Hess, E. P. and R. D. White (2004). "Recurrent ventricular fibrillation in out-of-hospital cardiac arrest after defibrillation by police and firefighters: implications for automated external defibrillator users." *Crit Care Med* 32(9 Suppl): S436-9.

LOE 4, fair, neutral. OHCA, retrospective cohort of VF treated by police or firefighters with biphasic (150J-150J-150J) AED. 1996-2003. N=67.

Recurrence of VF in 52%; not associated with survival, but no adjusted analysis undertaken.

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Hess, E. P., J. K. Russell, et al. (2008). "A high peak current 150-J fixed-energy defibrillation protocol treats recurrent ventricular fibrillation (VF) as effectively as initial VF." *Resuscitation*.

LOE 4, good, neutral. OHCA, retrospective cohort of patients treated with fixed low-dose biphasic AED. 1996-2007, N=103.

Shock success rate by shock number

Shock number	Shock success rate[5 sec] (%)
1	93/101 (92.1%)
2	58/63 (92.1%)
3	37/41 (90.2%)
4	18/21 (85.7%)
≥ 5	27/31 (87.1%)

Reported no loss in shock efficacy with increasing shock number. This analysis compared shock N+1 to N, but did not evaluate for evidence of statistical trend over range of shocks. Organized rhythm at 60 sec not reported.

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Higgins, S. L., J. M. Herre, et al. (2000). "A comparison of biphasic and monophasic shocks for external defibrillation. Physio-Control Biphasic Investigators." *Prehosp Emerg Care* 4(4): 305-13.

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) waveform 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.

Higgins, S. L., S. G. O'Grady, et al. (2004). "Efficacy of lower-energy biphasic shocks for transthoracic defibrillation: a follow-up clinical study." *Prehosp Emerg Care* 8(3): 262-7.

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.

Jakobsson, J., N. Rehnqvist, et al. (1989). "Energy requirement for early defibrillation." *Eur Heart J* 10(6): 551-4.

LOE 2, poor, neutral outcomes BE, opposed outcome C. 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%). No adjustments undertaken for differences in baseline or EMS-response characteristics.

Jones, J. L., J. F. Swartz, et al. (1990). "Increasing fibrillation duration enhances relative asymmetrical biphasic versus monophasic defibrillator waveform efficacy." *Circ Res* 67(2): 376-84.

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.

Killingsworth, C. R., S. B. Melnick, et al. (2002). "Defibrillation threshold and cardiac responses using an external biphasic defibrillator with pediatric and adult adhesive patches in pediatric-sized piglets." Resuscitation 55(2): 177-85.

LOE 5 (animal), poor, neutral. Prospective evaluation 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.

Koster, R. W., R. G. Walker, et al. (2006). "Definition of successful defibrillation." Crit Care Med 34(12 Suppl): S423-6.

LOE 4, good, neutral. 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%).

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Koster, R. W., R. G. Walker, et al. (2008). "Recurrent ventricular fibrillation during advanced life support care of patients with prehospital cardiac arrest." Resuscitation 78(3): 252-7.

LOE 4, good, supportive. OHCA, observational study of defibrillation efficacy of first and recurrent defibrillation. In the analysis limited to the first defibrillation attempt suggested increased defibrillation efficacy with a third shock at 360J (83%; 10/12) compared to the second shock at 200J (61%; 22/36). This trend was not statistically significant and the implications of escalating dose defibrillation among patients with recurrent ventricular fibrillation were not explored.

Kudenchuk, P. J., L. A. Cobb, et al. (2006). "Transthoracic Incremental Monophasic Versus Biphasic Defibrillation by Emergency Responders (TIMBER): A randomized comparison of monophasic with biphasic waveform ascending energy defibrillation for the resuscitation of out-of-hospital cardiac arrest due to ventricular fibrillation." Circulation 114(19): 2010-2018.

LOE 4, 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 (not further defined): 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%)

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Leng, C. T., N. A. Paradis, et al. (2000). "Resuscitation after prolonged ventricular fibrillation with use of monophasic and biphasic waveform pulses for external defibrillation." Circulation 101(25): 2968-74.

LOE 5 (animal), good, neutral. Randomized prospective non-blinded evaluation of escalating monophasic vs escalating biphasic defibrillation in a dog model. N=26.

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

No comparison of fixed dose to escalating dose biphasic defibrillation.

Lerman, B. B., H. R. Halperin, et al. (1987). "Relationship between canine transthoracic impedance and defibrillation threshold. Evidence for current-based defibrillation." J Clin Invest 80(3): 797-803.

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.

Mittal, S., S. Ayati, et al. (1999). "Comparison of a novel rectilinear biphasic waveform with a damped sine wave monophasic waveform for transthoracic ventricular defibrillation. ZOLL Investigators." J Am Coll Cardiol 34(5): 1595-601.

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.

First shock effective at terminating VF in 97/98 (99%) of patients receiving biphasic shock and 80/86 (93%, $p=0.05$) receiving monophasic.

Morgan, J. P., S. F. Hearne, et al. (1984). "High-energy versus low-energy defibrillation: experience in patients (excluding those in the intensive care unit) at Mayo Clinic-affiliated hospitals." Mayo Clin Proc 59(12): 829-34.

LOE 4, poor, supportive outcome E, neutral outcome 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%). Defibrillation efficacy was the same for second and third shocks regardless of starting energy level.

Morrison, L. J., P. Dorian, et al. (2005). "Out-of-hospital cardiac arrest rectilinear biphasic to monophasic damped sine defibrillation waveforms with advanced life support intervention trial (ORBIT)." Resuscitation 66(2): 149-157.

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.

Outcomes after one to three shocks:

Outcome	Biphasic	Monophasic	P-value
Organized rhythm (5 sec)	90/163 (55.2%)	66/149 (44.3%)	0.05
ROSC	61/164 (37.2%)	55/149 (36.9%)	0.25
Survival to discharge	8/163 (4.9%)	6/147 (4.1%)	"NS"

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Niemann, J. T., D. Burian, et al. (2000a). "Monophasic versus biphasic transthoracic countershock after prolonged ventricular fibrillation in a swine model." Journal of the American College of Cardiology 36(3): 932-938.

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.

No comparison of fixed dose to escalating dose biphasic defibrillation.

Niemann, J. T., D. Burian, et al. (2000b). "Transthoracic monophasic and biphasic defibrillation in a swine model: a comparison of efficacy, ST segment changes, and postshock hemodynamics." Resuscitation 47(1): 51-8.

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.

No comparison of fixed dose to escalating dose biphasic defibrillation.

Niemann, J. T., D. Garner, et al. (2003a). "Left ventricular function after monophasic and biphasic waveform defibrillation: The impact of cardiopulmonary resuscitation time on contractile indices." Academic Emergency Medicine 10(1): 9-15.

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.

Equal proportions achieved ROSC.

Niemann, J. T., D. Garner, et al. (2003b). "Transthoracic impedance does not decrease with rapidly repeated countershocks in a swine cardiac arrest model." Resuscitation 56(1): 91-5.

LOE 5 (animal), poor, neutral. Retrospective cohort of changes in transthoracic impedance in swine requiring more than 3 shocks for termination of VF of 5 min duration. N=13.

No change in transthoracic impedance with successive shocks.

Niemann, J. T., J. P. Rosborough, et al. (2004). "A model of ischemically induced ventricular fibrillation for comparison of fixed-dose and escalating-dose defibrillation strategies." Acad Emerg Med 11(6): 619-24.

LOE 5 (animal), good, supportive. Prospective, randomized, evaluation of fixed energy biphasic waveform (150J) compared to escalating energy (200-300-360J) transthoracic defibrillation in a swine model. Duration of VF=1 or 5 minutes. N=35.

Successful defibrillation with ≤ 3 shocks: fixed energy 5/17 (29%, 95% CI 10-56%), escalating energy 15/18 (83%, 95% CI 59-96%). Nine of the animals that could not be defibrillated with fixed energy were successfully defibrillated when treated with escalating energy.

Poole, J. E., R. D. White, et al. (1997). "Low-energy impedance-compensating biphasic waveforms terminate ventricular fibrillation at high rates in victims of out-of-hospital cardiac arrest. LIFE Investigators." J Cardiovasc Electrophysiol 8(12): 1373-85.

LOE 4, poor, neutral. OHCA, retrospective cohort of patients treated with biphasic 150J transthoracic defibrillation. 1996-1997. N=100

VF terminated with first shock in 39/44 (89%) and 100% within 3 shocks.

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Reddy, R. K., M. J. Gleva, et al. (1997). "Biphasic transthoracic defibrillation causes fewer ECG ST-segment changes after shock." Annals of Emergency Medicine 30(2): 127-134.

LOE 5 (at time of ICD testing), good, neutral. 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

Rossano, J. W., L. Quan, et al. (2006). "Energy doses for treatment of out-of-hospital pediatric ventricular fibrillation." Resuscitation 70(1): 80-89.

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

No comparison of fixed dose to escalating dose biphasic defibrillation.

Scheatzle, M. D., J. J. Menegazzi, et al. (1999). "Evaluation of biphasic transthoracic defibrillation in an animal model of prolonged ventricular fibrillation." Academic Emergency Medicine 6(9): 880-886.

LOE 5 (animal), poor, neutral. 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

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series in regards to LOE.

Schneider, T., P. R. Martens, et al. (2000). "Multicenter, randomized, controlled trial of 150-J biphasic shocks compared with 200- to 360-J monophasic shocks in the resuscitation of out-of-hospital cardiac arrest victims." Circulation 102(15): 1780-1787.

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). Underpowered for survival.

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

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

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Stiell, I. G., R. G. Walker, et al. (2007). "BIPHASIC trial: A randomized comparison of fixed lower versus escalating higher energy levels for defibrillation in out-of-hospital cardiac arrest." Circulation 115(12): 1511-1517.

LOE 1, good, supportive outcome E, neutral outcome ABCD. 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.

Outcomes clustered on single or multiple shocks	Fixed lower-energy	Escalating higher-energy	P-value
Termination VF (5sec)			
First shock only	99/114 (86.8%)	95/107 (88.8)	0.81
Multiple shocks	(71.2%)	(82.5%)	0.027
Organized rhythm (60sec)			
First shock only	28/112 (38.4%)	36/98 (36.7%)	0.92
Multiple shocks	(24.7%)	(36.6%)	0.035

Clinical Outcomes:

Outcome	Fixed lower-energy	Escalating higher-energy	P-value
ROSC	58/114 (50.9%)	52/107 (48.6%)	0.73

<i>Survival to discharge</i>	19/114 (16.7%)	17/107 (15.9%)	0.88
<i>Median Cerebral Performance Category scores (IQR)</i>	2 (1-3)	2(1-2)	0.72

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.

Stohtert, J. C., T. S. Hatcher, et al. (2004). "Rectilinear Biphasic Waveform Defibrillation of Out-of-hospital Cardiac Arrest." *Prehospital Emergency Care* 8(4): 388-392.

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. No comparison of fixed dose to escalating dose biphasic defibrillation.

Szili-Torok, T., D. Theuns, et al. (2002). "Transthoracic defibrillation of short-lasting ventricular fibrillation: a randomised trial for comparison of the efficacy of low-energy biphasic rectilinear and monophasic damped sine shocks." *Acta Cardiol* 57(5): 329-34.

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 fixed dose to escalating dose biphasic defibrillation.

Tang, W., M. H. Weil, et al. (1999). "The effects of biphasic and conventional monophasic defibrillation on postresuscitation myocardial function." *Journal of the American College of Cardiology* 34(3): 815-822.

LOE 5 (animal), good, neutral. 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. No comparison of fixed dose to escalating dose biphasic defibrillation.

Tang, W., M. H. Weil, et al. (2001). "A comparison of biphasic and monophasic waveform defibrillation after prolonged ventricular fibrillation." *Chest* 120(3): 948-954.

LOE 5 (animal), good, neutral. 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. No comparison of fixed dose to escalating dose biphasic defibrillation.

Tang, W., M. H. Weil, et al. (2002). "Fixed-energy biphasic waveform defibrillation in a pediatric model of cardiac arrest and resuscitation." *Critical Care Medicine* 30(12): 2736-2741.

LOE 5 (animal), poor, neutral. Prospective study of energy-reducing electrodes to deliver 50J biphasic shocks to piglet model of varying weights. Termination of VF and ROSC occurred in all animals evaluated. No comparison of fixed dose to escalating dose biphasic defibrillation.

Tang, W., M. H. Weil, et al. (2004). "The effects of biphasic waveform design on post-resuscitation myocardial function." *Journal of the American College of Cardiology* 43(7): 1228-1235.

LOE 5 (animal), good, neutral. Prospective, randomized evaluation of fixed-energy low-capacitance biphasic (150J or 200J) and high-capacitance biphasic (200J or 360J) defibrillation in a pig model. Duration VF = 7 min. N=20. Low-capacitance biphasic waveform resulted in termination of VF and survival in all samples and was associated with less myocardial dysfunction.

Tang, W., D. Snyder, et al. (2006). "One-shock versus three-shock defibrillation protocol significantly improves outcome in a porcine model of prolonged ventricular fibrillation cardiac arrest." *Circulation* 113(23): 2683-9.

LOE 5 (animal), good, supportive. Prospective randomized factorial design testing single shock vs 3-shock protocol and fixed dose biphasic (150-150-150J) vs escalating dose biphasic (200-300-360J) defibrillation in a pig model. N=44. Single shock protocol increased survival from 64% to 100% (95% CI of difference 19% to 58%, p=0.004). Between-group comparisons of 3-shock protocol demonstrated better survival with escalating dose biphasic defibrillation (91% vs 36%, p=0.024). No comparison of fixed dose to escalating dose biphasic defibrillation.

van Alem, A. P., F. W. Chapman, et al. (2003). "A prospective, randomised and blinded comparison of first shock success of monophasic and biphasic waveforms in out-of-hospital cardiac arrest." *Resuscitation* 58(1): 17-24.

LOE 4, good, neutral. 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 comparison of fixed dose to escalating dose biphasic defibrillation, thus considered a case series in regards to LOE.

Walcott, G. P., S. B. Melnick, et al. (1998). "Relative efficacy of monophasic and biphasic waveforms for transthoracic defibrillation after short and long durations of ventricular fibrillation." *Circulation* 98(20): 2210-5.

LOE 5 (animal), poor, neutral. Prospective evaluation 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.

Walcott, G. P., C. R. Killingsworth, et al. (2002). "Biphasic waveform external defibrillation thresholds for spontaneous ventricular fibrillation secondary to acute ischemia." *J Am Coll Cardiol* 39(2): 359-65.

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.

Walker, R. G., S. B. Melnick, et al. (2003). "Comparison of six clinically used external defibrillators in swine." *Resuscitation* 57(1): 73-83.

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 (150-150-150J), escalating high dose (200-300-360J), escalating low dose (120-150-200J) 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).

Walker, R. G., R. W. Koster, et al. (2009). "Defibrillation probability and impedance change between shocks during resuscitation from out-of-hospital cardiac arrest." *Resuscitation* 80(7): 773-7.

LOE 4, good, neutral. Observational cohort of out-of-hospital cardiac arrest requiring multiple shocks. In patients for whom 200J shock failed to terminate VF (n=61), 40% (N=2, 95% CI 5-85%) were terminated with a second shock of 200J compared to 70% (N=39, 95% CI 56-81%) converted with a second shock of 300J.

Walsh, S. J., A. J. McClelland, et al. (2004). "Efficacy of distinct energy delivery protocols comparing two biphasic defibrillators for cardiac arrest." *Am J Cardiol* 94(3): 378-80.

LOE 2, fair, supportive. 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).

Termination VF (5sec):

Shock	Escalating dose (N=79)	Fixed dose (N=95)	P-value
1	46 (58%)	61 (64%)	"NS"
2	65 (82%)	74 (78%)	"NS"
3	73 (92%)	79 (83%)	0.029

White, R. D. (1997). "Early out-of-hospital experience with an impedance-compensating low-energy biphasic waveform automatic external defibrillator." *J Interv Card Electrophysiol* 1(3): 203-8; discussion 209-10.

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 fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

White, R. D., D. G. Hankins, et al. (2001). "Patient outcomes following defibrillation with a low energy biphasic truncated exponential waveform in out-of-hospital cardiac arrest." *Resuscitation* 49(1): 9-14.

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 fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

White, R. D. and J. K. Russell (2002). "Refrillation, resuscitation and survival in out-of-hospital sudden cardiac arrest victims treated with biphasic automated external defibrillators." Resuscitation 55(1): 17-23.

LOE 4, fair, neutral. OHCA, retrospective cohort evaluating incidence of refrillation and outcome in management of VF OHCA treated with fixed dose (150-150-150J) biphasic defibrillation. 1996-2001. N=49.

Although refrillation occurred frequently (61%), it was not associated with ROSC, survival to discharge, or neurologically intact survival.

No comparison of fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

White, R. D., T. H. Blackwell, et al. (2004). "Body weight does not affect defibrillation, resuscitation, or survival in patients with out-of-hospital cardiac arrest treated with a nonescalating biphasic waveform defibrillator." Crit Care Med 32(9 Suppl): S387-92.

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 fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

White, R. D., T. H. Blackwell, et al. (2005). "Transthoracic impedance does not affect defibrillation, resuscitation or survival in patients with out-of-hospital cardiac arrest treated with a non-escalating biphasic waveform defibrillator." Resuscitation 64(1): 63-69.

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 fixed dose to escalating dose biphasic defibrillation, thus considered case series for LOE.

Xie, J., M. H. Weil, et al. (1997). "High-energy defibrillation increases the severity of postresuscitation myocardial dysfunction." Circulation 96(2): 683-688.

LOE 5 (animal), good, neutral. 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.

No evaluation of multiple shocks or comparison of fixed dose to escalating dose biphasic defibrillation.

Yamaguchi, H., M. Weil, et al. (2002). "Myocardial dysfunction after electrical defibrillation." Resuscitation 54(3): 289-96.

LOE 5 (animal), good, neutral. Prospective randomized non-blinded evaluation of myocardial ischemia on post-shock dysfunction with varying energy levels (0.4 and 0.7J) in a isolated rat heart model. Duration VF = 10 to 15 min. N=50. Post-shock myocardial dysfunction only observed in ischemic rat heart model.

No evaluation of multiple shocks or comparison of fixed dose to escalating dose biphasic defibrillation.

Yamanouchi, Y., J. E. Brewer, et al. (1999). "External exponential biphasic versus monophasic shock waveform: efficacy in ventricular fibrillation of longer duration." Pacing Clin Electrophysiol 22(10): 1481-7.

LOE 5 (animal), poor, neutral. Prospective evaluation 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 within waveforms for different durations of VF arrest.

Zelinka, M., D. Buic, et al. (2007). "Comparison of five different defibrillators using recommended energy protocols." Resuscitation 74(3): 500-7.

LOE 5 (resistive load model), poor, supportive. Prospective study of five different defibrillator electrical properties when discharged into resistive loads of 50, 90, and 130 Ohms. Current amplitude lower than expected when discharged into larger resistive loads despite impedance compensating defibrillators.

Zhang, Y., G. Karlsson, et al. (2001). "Biphasic and monophasic transthoracic defibrillation in pigs with acute left ventricular dysfunction." Resuscitation 50(1): 95-101.

LOE 5 (animal), good, neutral. 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.

No comparison of fixed dose to escalating dose biphasic defibrillation.

Zhang, Y., C. B. Clark, et al. (2002). "Body weight is a predictor of biphasic shock success for low energy transthoracic defibrillation." Resuscitation 54(3): 281-7.

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.

Zhang, Y., R. S. Ramabadran, et al. (2003). "Triphasic waveforms are superior to biphasic waveforms for transthoracic defibrillation: experimental studies." J Am Coll Cardiol 42(3): 568-75.

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.